

77258

Access DB#

## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: BERCH Examiner #: 59193 Date: 10/4  
 Art Unit: 1624 Phone Number 30 8478 Serial Number: 101081826  
 Mail Box and Bldg/Room Location: 4D15 Results Format Preferred (circle): PAPER DISK E-MAIL  
4E12

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

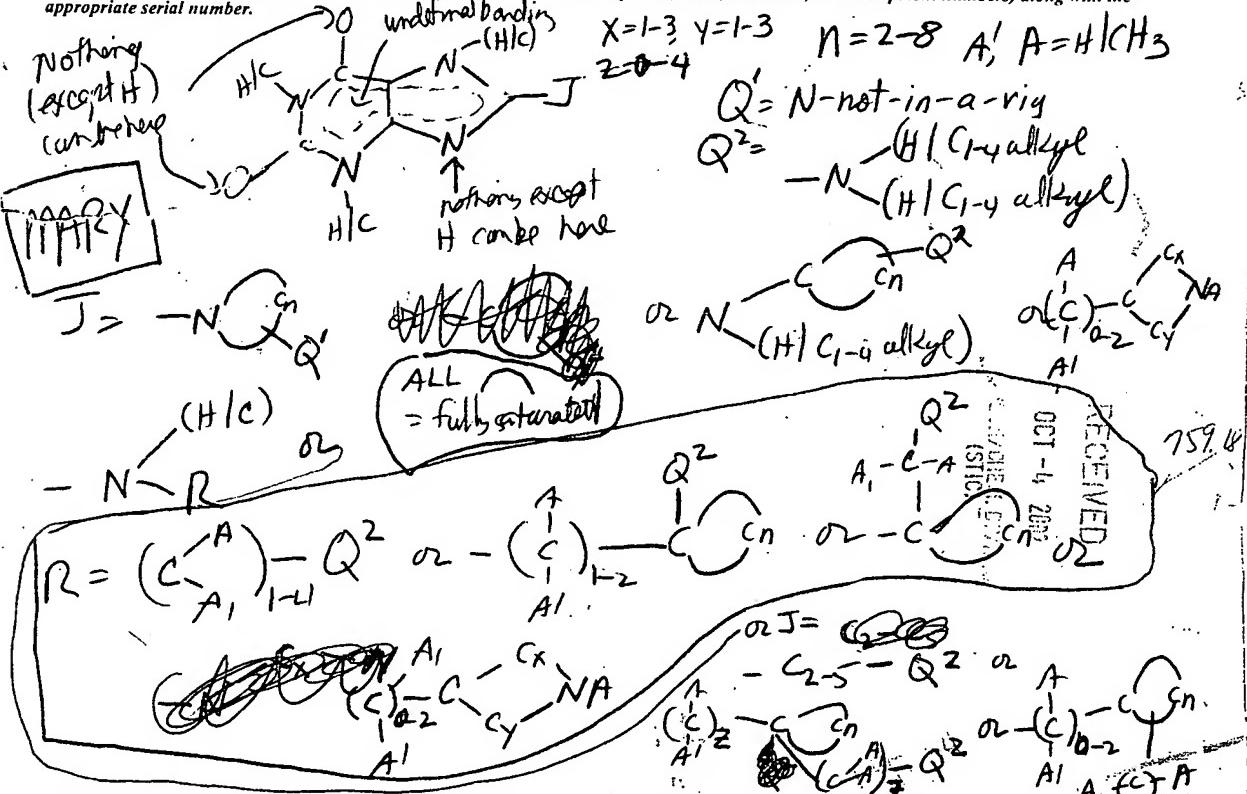
Crowdred  
Art!

Title of Invention:

Inventors (please provide full names):

Earliest Priority Filing Date:

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



## STAFF USE ONLY

Searcher: Mary

## Type of Search

Searcher Phone #:

NA Sequence (#)

Searcher Location:

AA Sequence (#)

Date Searcher Picked Up:

Structure (#)

Date Completed: 12/3

Bibliographic

Searcher Prep &amp; Review Time:

Litigation

Clerical Prep Time:

Fulltext

Online Time: 82

Patent Family

## Vendors and cost where applicable

STN 3269 Q<sup>2</sup>

Dialog \_\_\_\_\_

Questel/Orbit \_\_\_\_\_

Dr.Link \_\_\_\_\_

Lexis/Nexis \_\_\_\_\_

Sequence Systems \_\_\_\_\_

WWW/Internet \_\_\_\_\_

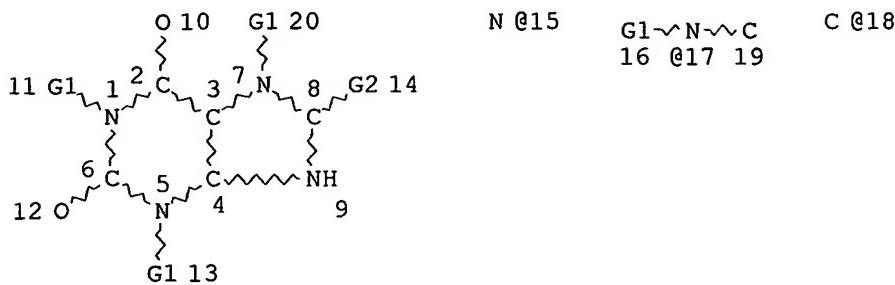
Other (specify) \_\_\_\_\_

L5

L18

Berth  
10/08/826

=> d 111 que stat;d 1-5 ide cbib abs  
L1 STR



VAR G1=H/C

VAR G2=15/17/18

NODE ATTRIBUTES:

NSPEC IS R AT 15  
NSPEC IS RC AT 18  
NSPEC IS RC AT 19  
CONNECT IS M1 RC AT 10  
CONNECT IS M1 RC AT 12  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

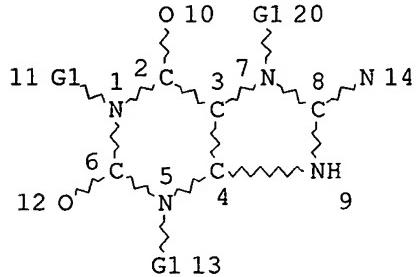
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE

L3 5409 SEA FILE=REGISTRY SSS FUL L1  
L4 STR



VAR G1=H/C

NODE ATTRIBUTES:

NSPEC IS R AT 14  
CONNECT IS M1 RC AT 10  
CONNECT IS M1 RC AT 12  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

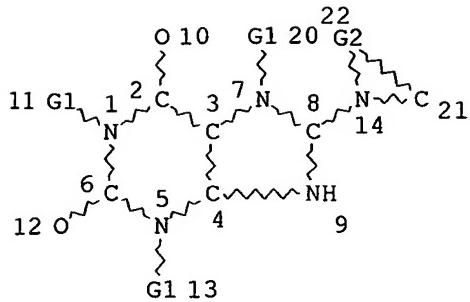
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

L5 80 SEA FILE=REGISTRY SUB=L3 SSS FUL L4  
L8 STR



```

VAR G1=H/C
REP G2=(0-7) C
NODE ATTRIBUTES:
NSPEC IS R AT 14
CONNECT IS M1 RC AT 10
CONNECT IS M1 RC AT 12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

```

```

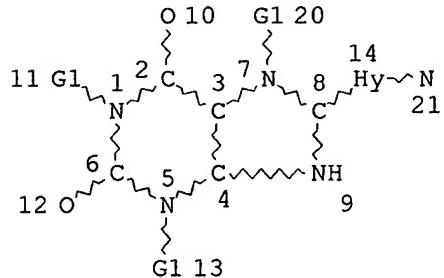
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

```

```

STEREO ATTRIBUTES: NONE
L9 51 SEA FILE=REGISTRY SUB=L5 SSS FUL L8
L10 STR

```



```

VAR G1=H/C
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 10
CONNECT IS M1 RC AT 12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

```

```

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

```

```

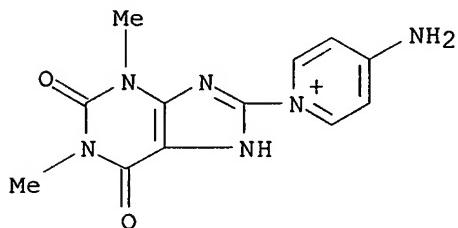
STEREO ATTRIBUTES: NONE
L11 5 SEA FILE=REGISTRY SUB=L9 SSS FUL L10

```

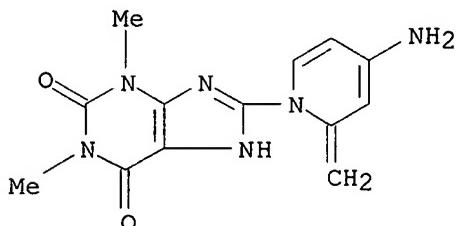
100.0% PROCESSED 51 ITERATIONS  
SEARCH TIME: 00.00.01

5 ANSWERS

L11 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2002 ACS  
RN 400880-39-9 REGISTRY  
CN Pyridinium, 4-amino-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C12 H13 N6 O2  
CI COM  
SR Chemical Library  
LC STN Files: CHEMCATS

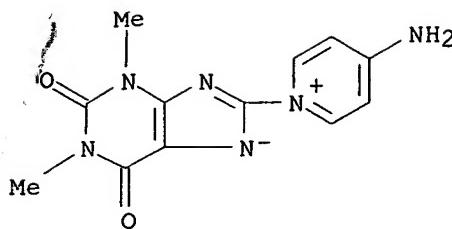


L11 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2002 ACS  
RN 374698-74-5 REGISTRY  
CN 1H-Purine-2,6-dione, 8-(4-amino-2-methylene-1(2H)-pyridinyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C13 H14 N6 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L11 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2002 ACS  
RN 331230-68-3 REGISTRY  
CN Pyridinium, 4-amino-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C12 H12 N6 O2  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS

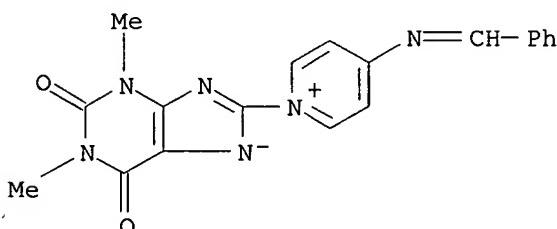


1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:252191 Reactions of theophyllines. Chemical conversions of 8-aminotheophyllinates. Kuz'menko, I. I.; Zvolinskaya, T. V. (Institute of Pharmacology and Toxicology, Ukrainian Academy of Medicinal Sciences, Kiev, 252057, Ukraine). Chemistry of Heterocyclic Compounds (New York) (Translation of Khimiya Geterotsiklichesikh Soedinenii), Volume Date 2000, 36(8), 963-970 (English) 2001. CODEN: CHCCAL. ISSN: 0009-3122. Publisher: Consultants Bureau.

AB Thermally stable, colored 8-aminotheophyllinates (betaine derivs. of theophylline) form unstable, colorless salts with strong mineral acids and undergo partial decompn. to a uric acid upon prolonged refluxing with concd. base soln. Substituted 8-pyridinium theophyllinates readily take part in typical reactions of the functional group in the substituted pyridine ring with retention of the betaine structure. The formation of the synthesized compds. was confirmed by IR and NMR spectroscopy.

L11 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2002 ACS  
 RN 331230-60-5 REGISTRY  
 CN Pyridinium, 4-[(phenylmethylene)amino]-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C19 H16 N6 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT



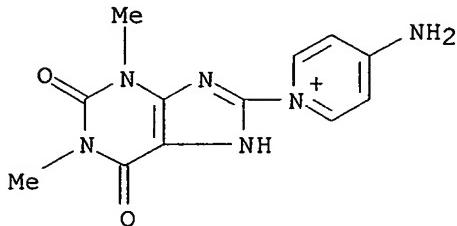
1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:252191 Reactions of theophyllines. Chemical conversions of 8-aminotheophyllinates. Kuz'menko, I. I.; Zvolinskaya, T. V. (Institute of Pharmacology and Toxicology, Ukrainian Academy of Medicinal Sciences, Kiev, 252057, Ukraine). Chemistry of Heterocyclic Compounds (New York) (Translation of Khimiya Geterotsiklichesikh Soedinenii), Volume Date 2000, 36(8), 963-970 (English) 2001. CODEN: CHCCAL. ISSN: 0009-3122. Publisher: Consultants Bureau.

AB Thermally stable, colored 8-aminotheophyllinates (betaine derivs. of

theophylline) form unstable, colorless salts with strong mineral acids and undergo partial decompn. to a uric acid upon prolonged refluxing with concd. base soln. Substituted 8-pyridinium theophyllinates readily take part in typical reactions of the functional group in the substituted pyridine ring with retention of the betaine structure. The formation of the synthesized compds. was confirmed by IR and NMR spectroscopy.

L11 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2002 ACS  
RN 331230-59-2 REGISTRY  
CN Pyridinium, 4-amino-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, chloride (9CI) (CA INDEX NAME)  
MF C12 H13 N6 O2 . Cl  
SR CA  
LC STN Files: CA, CAPLUS  
CRN (400880-39-9)



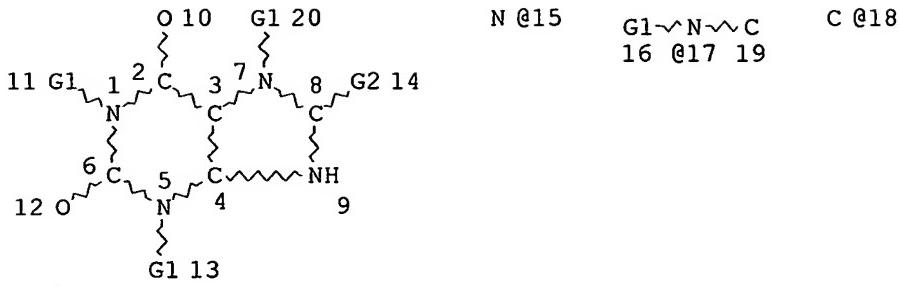
● Cl<sup>-</sup>

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:252191 Reactions of theophyllines. Chemical conversions of 8-aminothеophyllinates. Kuz'menko, I. I.; Zvolinskaya, T. V. (Institute of Pharmacology and Toxicology, Ukrainian Academy of Medicinal Sciences, Kiev, 252057, Ukraine). Chemistry of Heterocyclic Compounds (New York) (Translation of Khimiya Geterotsiklicheskikh Soedinenii), Volume Date 2000, 36(8), 963-970 (English) 2001. CODEN: CHCCAL. ISSN: 0009-3122. Publisher: Consultants Bureau.

AB Thermally stable, colored 8-aminothеophyllinates (betaine derivs. of theophylline) form unstable, colorless salts with strong mineral acids and undergo partial decompn. to a uric acid upon prolonged refluxing with concd. base soln. Substituted 8-pyridinium theophyllinates readily take part in typical reactions of the functional group in the substituted pyridine ring with retention of the betaine structure. The formation of the synthesized compds. was confirmed by IR and NMR spectroscopy.

=> d 115 que stat  
L1 STR



```

VAR G1=H/C
VAR G2=15/17/18
NODE ATTRIBUTES:
NSPEC IS R AT 15
NSPEC IS RC AT 18
NSPEC IS RC AT 19
CONNECT IS M1 RC AT 10
CONNECT IS M1 RC AT 12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

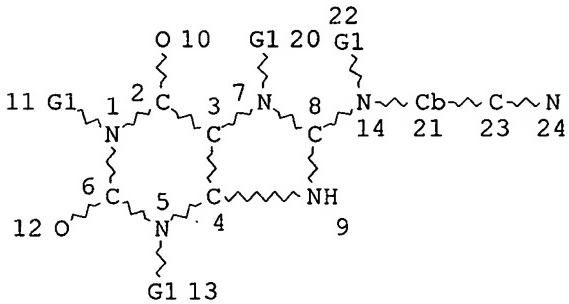
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

```

```

STEREO ATTRIBUTES: NONE
L3 5409 SEA FILE=REGISTRY SSS FUL L1
L26 STR

```



```

VAR G1=H/C
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 10
CONNECT IS M1 RC AT 12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

```

```

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

```

```

STEREO ATTRIBUTES: NONE
L27 0 SEA FILE=REGISTRY SUB=L3 SSS FUL L26

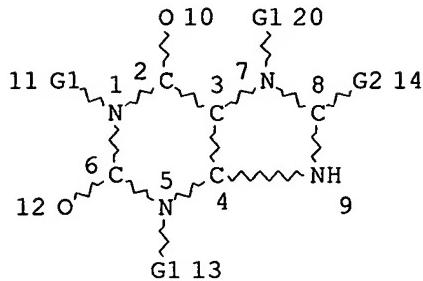
```

```

100.0% PROCESSED 552 ITERATIONS
SEARCH TIME: 00.00.01
0 ANSWERS

```

```
=> d 129 que stat;d 1-177 ide cbib abs  
L1 STR
```



```
VAR G1=H/C  
VAR G2=15/17/18  
NODE ATTRIBUTES:
```

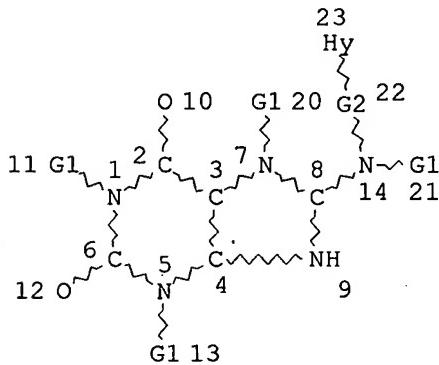
```
NSPEC IS R AT 15  
NSPEC IS RC AT 18  
NSPEC IS RC AT 19  
CONNECT IS M1 RC AT 10  
CONNECT IS M1 RC AT 12  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED
```

```
GRAPH ATTRIBUTES:
```

```
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 20
```

```
STEREO ATTRIBUTES: NONE
```

```
L3 5409 SEA FILE=REGISTRY SSS FUL L1  
L28 STR
```



```
VAR G1=H/C  
REP G2=(0-2) C  
NODE ATTRIBUTES:  
CONNECT IS M1 RC AT 10  
CONNECT IS M1 RC AT 12  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED
```

```
GRAPH ATTRIBUTES:
```

```
RING(S) ARE ISOLATED OR EMBEDDED
```

NUMBER OF NODES IS 18

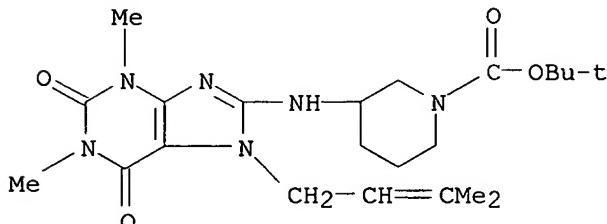
STEREO ATTRIBUTES: NONE

L29 177 SEA FILE=REGISTRY SUB=L3 SSS FUL L28

100.0% PROCESSED 2277 ITERATIONS  
SEARCH TIME: 00.00.01

177 ANSWERS

L29 ANSWER 1 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 454709-35-4 REGISTRY  
CN 1-Piperidinecarboxylic acid, 3-[(2,3,6,7-tetrahydro-1,3-dimethyl-7-(3-methyl-2-butenyl)-2,6-dioxo-1H-purin-8-yl)amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H34 N6 O4  
SR CA  
LC STN Files: CA, CAPLUS

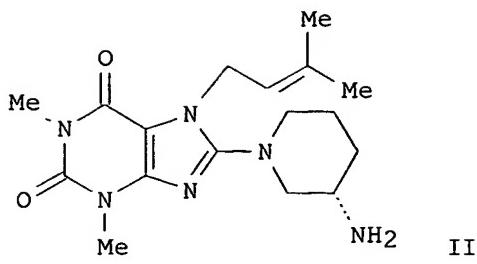
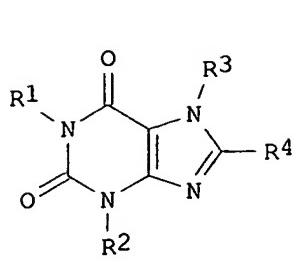


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:216824 Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1 20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE 2002-10203486 20020130.

GI



AB Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical compns. contg. I are described. Thus, II was prep'd. and had an IC<sub>50</sub> of 22 nM against dipeptidylpeptidase-IV.

L29 ANSWER 2 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 454709-34-3 REGISTRY

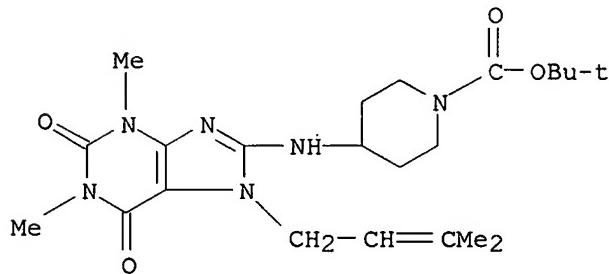
CN 1-Piperidinocarboxylic acid, 4-[(2,3,6,7-tetrahydro-1,3-dimethyl-7-(3-methyl-2-butenyl)-2,6-dioxo-1H-purin-8-yl)amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H34 N6 O4

SR CA

LC STN Files: CA, CAPLUS



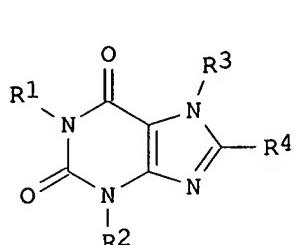
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

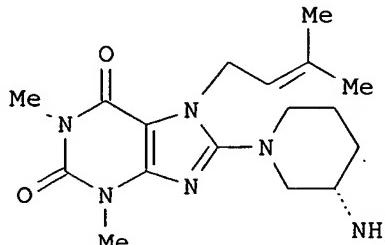
REFERENCE 1: 137:216824 Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1 20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT,

LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2.  
 APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021  
 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE  
 2002-10203486 20020130.

GI



I



II

AB Xanthine derivs. of formula I [R<sub>1</sub>, R<sub>2</sub> = H, alkyl, alkenyl, etc.; R<sub>3</sub> = alkyl, arylalkyl, etc.; R<sub>4</sub> = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical compns. contg. I are described. Thus, II was prep'd. and had an IC<sub>50</sub> of 22 nM against dipeptidylpeptidase-IV.

L29 ANSWER 3 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 454709-31-0 REGISTRY

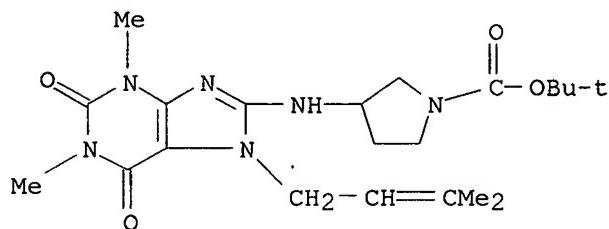
CN 1-Pyrrolidinecarboxylic acid, 3-[[2,3,6,7-tetrahydro-1,3-dimethyl-7-(3-methyl-2-butenyl)-2,6-dioxo-1H-purin-8-yl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C21 H32 N6 O4

SR CA

LC STN Files: CA, CAPLUS



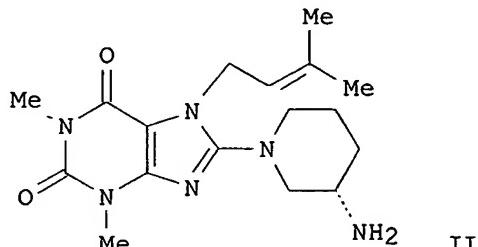
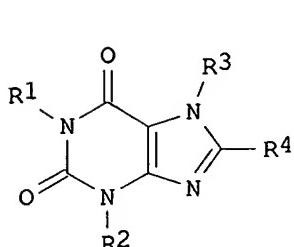
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:216824 Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1 20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,

KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2.  
 APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021  
 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE  
 2002-10203486 20020130.

GI



AB Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical compns. contg. I are described. Thus, II was prep'd. and had an IC<sub>50</sub> of 22 nM against dipeptidylpeptidase-IV.

L29 ANSWER 4 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 454707-31-4 REGISTRY

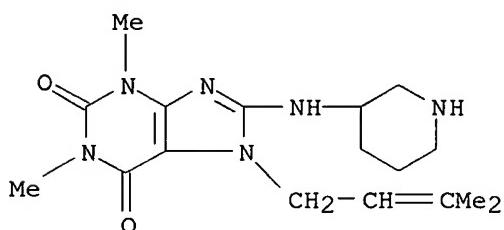
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(3-methyl-2-butenyl)-8-(3-piperidinylamino)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C17 H26 N6 O2

SR CA

LC STN Files: CA, CAPLUS



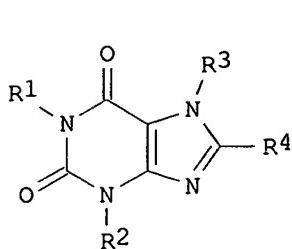
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

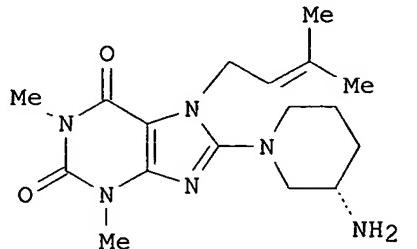
REFERENCE 1: 137:216824 Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1

20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE 2002-10203486 20020130.

GI



I



II

AB Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical compns. contg. I are described. Thus, II was prep'd. and had an IC<sub>50</sub> of 22 nM against dipeptidylpeptidase-IV.

L29 ANSWER 5 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 454707-30-3 REGISTRY

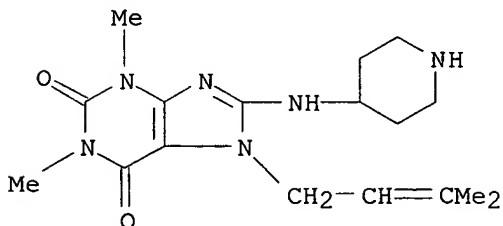
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(3-methyl-2-butenyl)-8-(4-piperidinylamino)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C17 H26 N6 O2

SR CA

LC STN Files: CA, CAPLUS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

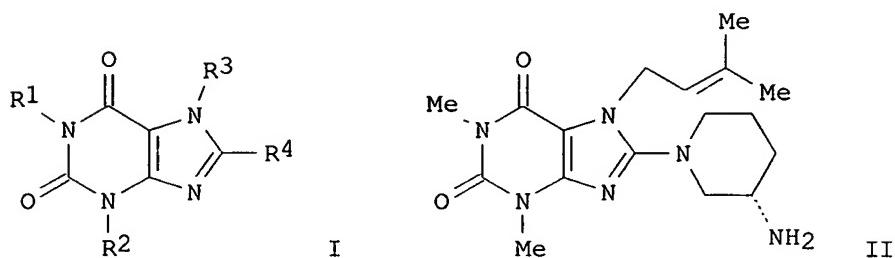
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:216824 Preparation of xanthine derivatives as

Searched by: Mary Hale 308-4258 CM-1 1E01

dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1 20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE 2002-10203486 20020130.

GI



AB Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical comps. contg. I are described. Thus, II was prep'd. and had an IC<sub>50</sub> of 22 nM against dipeptidylpeptidase-IV.

L29 ANSWER 6 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 454707-22-3 REGISTRY

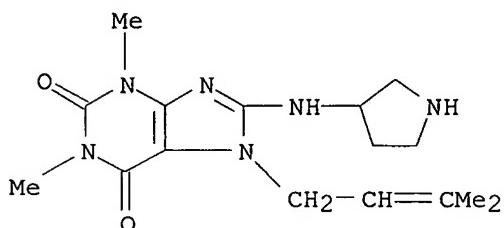
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(3-methyl-2-butenyl)-8-(3-pyrrolidinylamino)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C16 H24 N6 Q2

SR CA

LC STN Files: CA- CAPIUS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

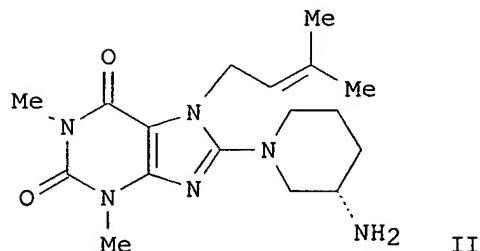
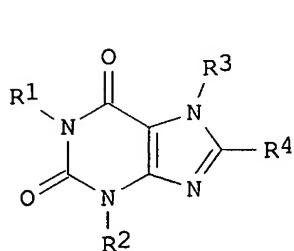
1 REFERENCES IN FILE CA (1962 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 1E01

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:216824 Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1 20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE 2002-10203486 20020130.

GI



**AB** Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical comps. contg. I are described. Thus, II was prep'd. and had an IC<sub>50</sub> of 22 nM against dipeptidylpeptidase-IV.

L29 ANSWER 7 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 454706-38-8 REGISTRY

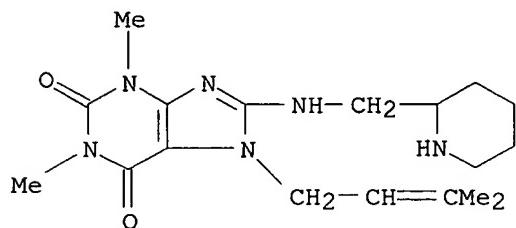
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(  
piperidinylmethyl)amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C18 H28 N6 O2

SR CA

LC STN Files: CA, CAPLUS

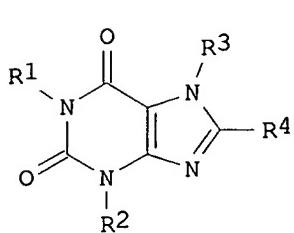


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

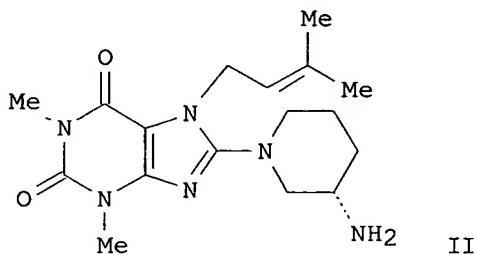
1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:216824 Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1 20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE 2002-10203486 20020130.

GI



I



II

AB Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical compns. contg. I are described. Thus, II was prep'd. and had an IC50 of 22 nM against dipeptidylpeptidase-IV.

L29 ANSWER 8 OF 177 REGISTRY COPYRIGHT 2002 ACS

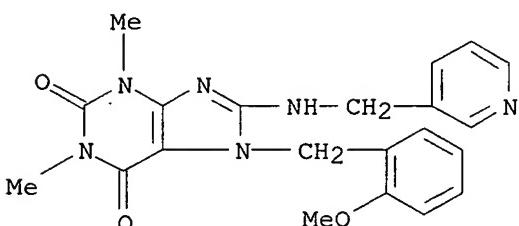
RN 443905-25-7 REGISTRY

CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[(2-methoxyphenyl)methyl]-1,3-dimethyl-8-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C21 H22 N6 O3

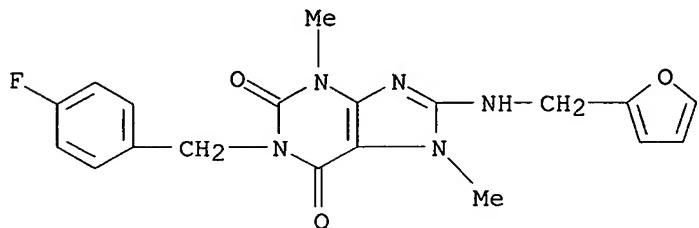
SR Chemical Library



Searched by: Mary Hale 308-4258 CM-1 1E01

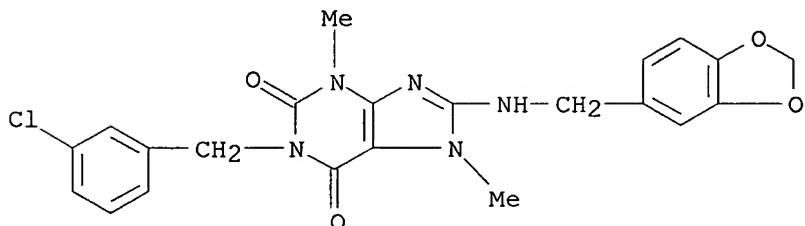
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 9 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 443904-06-1 REGISTRY  
CN 1H-Purine-2,6-dione; 1-[(4-fluorophenyl)methyl]-8-[(2-furanyl methyl)amino]-  
3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 F N5 O3  
SR Chemical Library



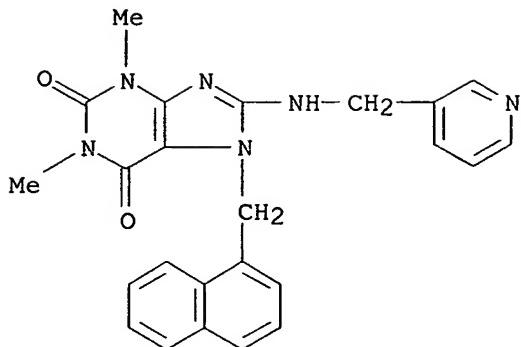
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 10 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 443903-74-0 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-1-[(3-chlorophenyl)methyl]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H20 Cl N5 O4  
SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 11 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 441288-48-8 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(1-naphthalenylmethyl)-8-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C24 H22 N6 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 12 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 441288-45-5 REGISTRY

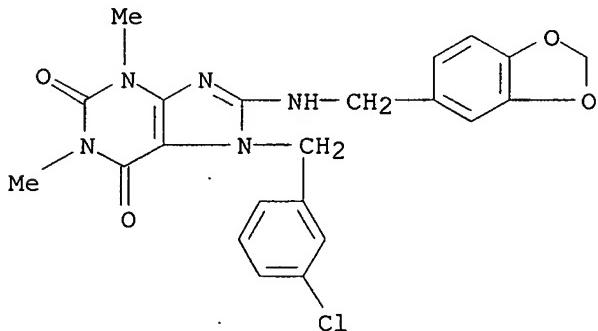
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(3-chlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H20 Cl N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 13 OF 177 REGISTRY COPYRIGHT 2002 ACS

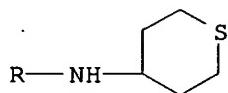
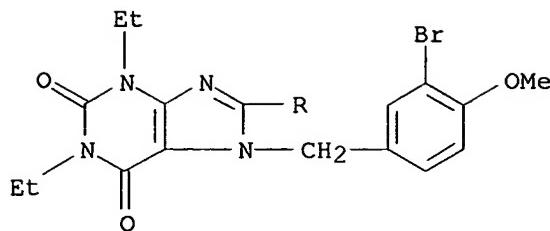
RN 405215-47-6 REGISTRY

CN 1H-Purine-2,6-dione, 7-[(3-bromo-4-methoxyphenyl)methyl]-1,3-diethyl-3,7-dihydro-8-[(tetrahydro-2H-thiopyran-4-yl)amino]- (9CI) (CA INDEX NAME)

MF C22 H28 Br N5 O3 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
 APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567  
 20000919.

GI

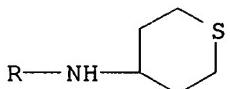
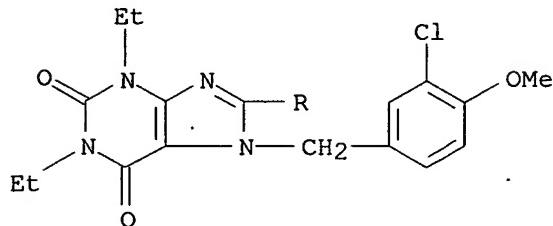
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO2H, CHO, CONH2, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degrees..

L29 ANSWER 14 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 405215-46-5 REGISTRY

Searched by: Mary Hale 308-4258 CM-1 1E01

CN 1H-Purine-2,6-dione, 7-[(3-chloro-4-methoxyphenyl)methyl]-1,3-diethyl-3,7-dihydro-8-[(tetrahydro-2H-thiopyran-4-yl)amino]- (9CI) (CA INDEX NAME)  
MF C22 H28 Cl N5 O3 S  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567 20000919.

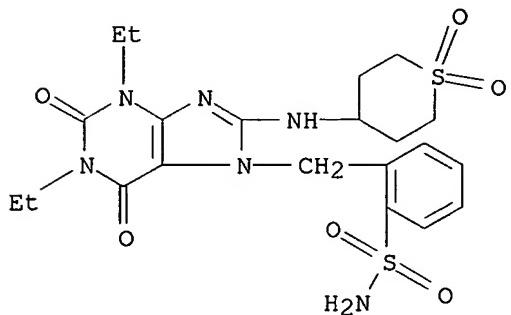
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO2H, CHO, CONH2, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the

title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube at 160.degree..

L29 ANSWER 15 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 405215-45-4 REGISTRY  
CN Benzenesulfonamide, 2-[(1,3-diethyl-1,2,3,6-tetrahydro-2,6-dioxo-8-[(tetrahydro-1,1-dioxido-2H-thiopyran-4-yl)amino]-7H-purin-7-yl)methyl]-(9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C21 H28 N6 O6 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567 20000919.

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO2H, CHO, CONH2, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug

are prepd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prepd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 16 OF 177 REGISTRY COPYRIGHT 2002 ACS

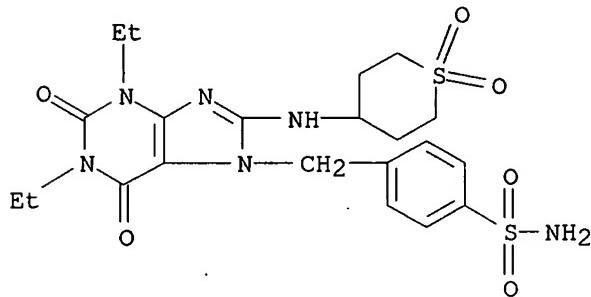
RN 405215-44-3 REGISTRY

CN Benzenesulfonamide, 4-[(1,3-diethyl-1,2,3,6-tetrahydro-2,6-dioxo-8-[(tetrahydro-1,1-dioxido-2H-thiopyran-4-yl)amino]-7H-purin-7-yl)methyl]-(9CI) (CA INDEX NAME)

MF C21 H28 N6 O6 S2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.

APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567 20000919.

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO2H, CHO, CONH2, H; R3 = aryl,

heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 17 OF 177 REGISTRY COPYRIGHT 2002 ACS

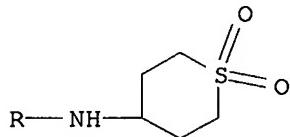
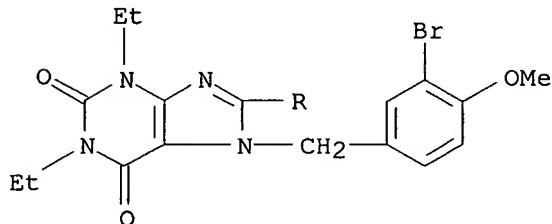
RN 405215-43-2 REGISTRY

CN 1H-Purine-2,6-dione, 7-[(3-bromo-4-methoxyphenyl)methyl]-1,3-diethyl-3,7-dihydro-8-[(tetrahydro-1,1-dioxido-2H-thiopyran-4-yl)amino]- (9CI) (CA INDEX NAME)

MF C22 H28 Br N5 O5 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567 20000919.

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO<sub>2</sub>H, CHO, CONH<sub>2</sub>, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 18 OF 177 REGISTRY COPYRIGHT 2002 ACS

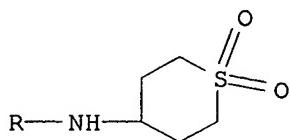
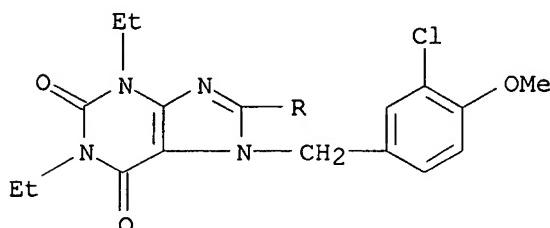
RN 405215-42-1 REGISTRY

CN 1H-Purine-2,6-dione, 7-[(3-chloro-4-methoxyphenyl)methyl]-1,3-diethyl-3,7-dihydro-8-[(tetrahydro-1,1-dioxido-2H-thiopyran-4-yl)amino]- (9CI) (CA INDEX NAME)

MF C22 H28 Cl N5 O5 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W:

AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS,  
JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO,  
NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ,  
VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF,  
CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML,  
MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567  
20000919.

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO<sub>2</sub>H, CHO, CONH<sub>2</sub>, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prepd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prepd. from bromothephylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 19 OF 177 REGISTRY COPYRIGHT 2002 ACS

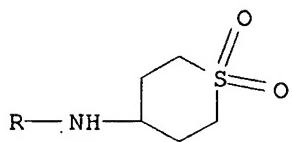
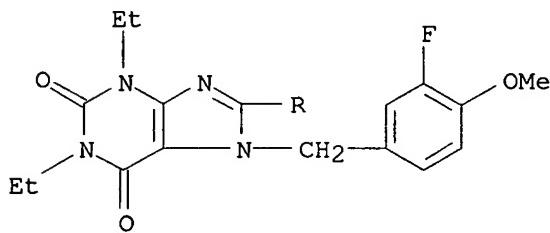
RN 405215-41-0 REGISTRY

CN 1H-Purine-2,6-dione, 1,3-diethyl-7-[(3-fluoro-4-methoxyphenyl)methyl]-3,7-dihydro-8-[(tetrahydro-1,1-dioxido-2H-thiopyran-4-yl)amino]- (9CI) (CA INDEX NAME)

MF C22 H28 F N5 O5 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567  
20000919.

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO<sub>2</sub>H, CHO, CONH<sub>2</sub>, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube at 160.degree..

L29 ANSWER 20 OF 177 REGISTRY COPYRIGHT 2002 ACS

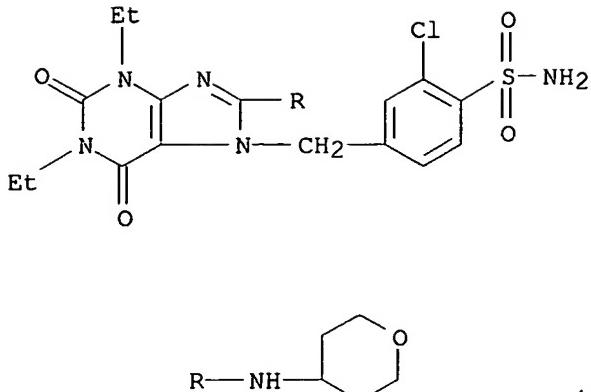
RN 405215-40-9 REGISTRY

CN Benzenesulfonamide, 2-chloro-4-[[1,3-diethyl-1,2,3,6-tetrahydro-2,6-dioxo-8-[(tetrahydro-2H-pyran-4-yl)amino]-7H-purin-7-yl]methyl]- (9CI) (CA INDEX NAME)

MF C21 H27 Cl N6 O5 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567  
20000919.

GI

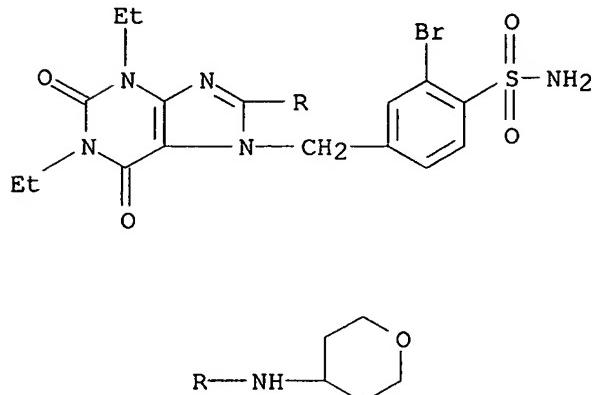
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO2H, CHO, CONH2, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prepd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prepd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 21 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 405215-39-6 REGISTRY

Searched by: Mary Hale 308-4258 CM-1 1E01

CN Benzenesulfonamide, 2-bromo-4-[(1,3-diethyl-1,2,3,6-tetrahydro-2,6-dioxo-8-[(tetrahydro-2H-pyran-4-yl)amino]-7H-purin-7-yl)methyl] - (9CI) (CA INDEX NAME)  
 MF C21 H27 Br N6 O5 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
 APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567 20000919.

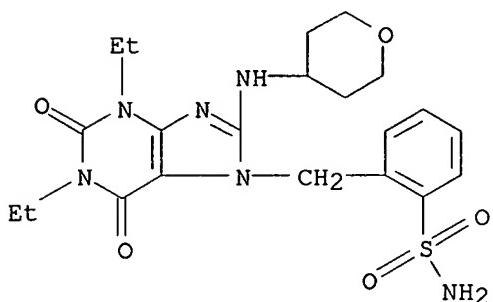
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO<sub>2</sub>H, CHO, CONH<sub>2</sub>, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid,

.alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube at 160.degree..

L29 ANSWER 22 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 405215-38-5 REGISTRY  
CN Benzenesulfonamide, 2-[[1,3-diethyl-1,2,3,6-tetrahydro-2,6-dioxo-8-[(tetrahydro-2H-pyran-4-yl)amino]-7H-purin-7-yl]methyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C21 H28 N6 O5 S  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567 20000919.

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO2H, CHO, CONH2, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or

more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 23 OF 177 REGISTRY COPYRIGHT 2002 ACS

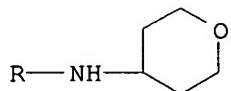
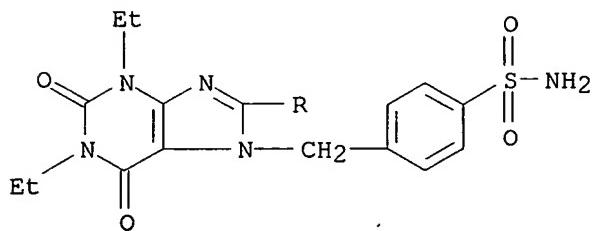
RN 405215-37-4 REGISTRY

CN Benzenesulfonamide, 4-[(1,3-diethyl-1,2,3,6-tetrahydro-2,6-dioxo-8-[(tetrahydro-2H-pyran-4-yl)amino]-7H-purin-7-yl)methyl]- (9CI) (CA INDEX NAME)

MF C21 H28 N6 O5 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567  
20000919.

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO<sub>2</sub>H, CHO, CONH<sub>2</sub>, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 24 OF 177 REGISTRY COPYRIGHT 2002 ACS

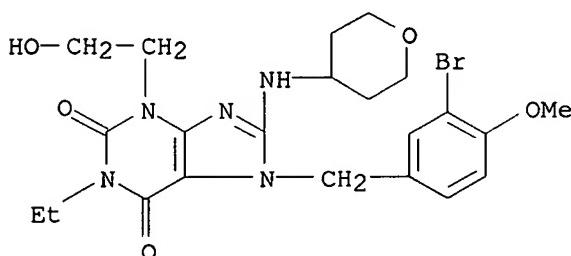
RN 405214-64-4 REGISTRY

CN 1H-Purine-2,6-dione, 7-[(3-bromo-4-methoxyphenyl)methyl]-1-ethyl-3,7-dihydro-3-(2-hydroxyethyl)-8-[(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

MF C22 H28 Br N5 O5

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567  
20000919.

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO<sub>2</sub>H, CHO, CONH<sub>2</sub>, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 25 OF 177 REGISTRY COPYRIGHT 2002 ACS

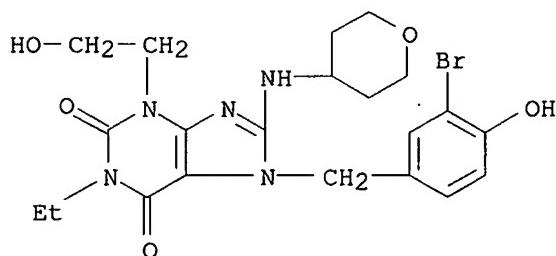
RN 405214-54-2 REGISTRY

CN 1H-Purine-2,6-dione, 7-[(3-bromo-4-hydroxyphenyl)methyl]-1-ethyl-3,7-dihydro-3-(2-hydroxyethyl)-8-[(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

MF C21 H26 Br N5 O5

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:263171 Preparation of arylmethyl-1H-purine-2,6-diones as xanthine phosphodiesterase V inhibitors. Chackalamannil, Samuel; Wang, Yuguang; Boyle, Craig D.; Stamford, Andrew W. (Schering Corporation, USA). PCT Int. Appl. WO 2002024698 A1 20020328, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-US28983 20010917. PRIORITY: US 2000-PV233567  
20000919.

GI

Searched by: Mary Hale 308-4258 CM-1 1E01

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; R1, R2 independently = C1-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, C3-15 cycloalkyl, heteroaryl, OH, CO<sub>2</sub>H, CHO, CONH<sub>2</sub>, H; R3 = aryl, heteroaryl; R4 = C3-15 cycloalkyl with or without one or more substituents, C3-15 cycloalkenyl, with or without one or more substituents, heterocycloalkyl of 3 to 15 members, with or without one or more substituents], enantiomers, stereoisomers, tautomers and/or prodrug are prep'd. as xanthine phosphodiesterase V inhibitors and are useful for treating male (erectile) and female sexual dysfunction and other physiol. disorders. Method for treating disorders including title compds. I and/or with nitrate donating pharmaceutical compn. and comprising a prostanoid, .alpha.-adrenergic receptor, dopamine receptor agonist, etc. Thus, the title compd. II was prep'd. from bromotheophylline, 6-chloropiperonyl chloride, and cyclohexylamine in the presence of 1-methyl-2-pyrrolidinone (NMP) and diisopropylethylamine (DIPEA) in sealed tube ate 160.degree..

L29 ANSWER 26 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 402506-05-2 REGISTRY

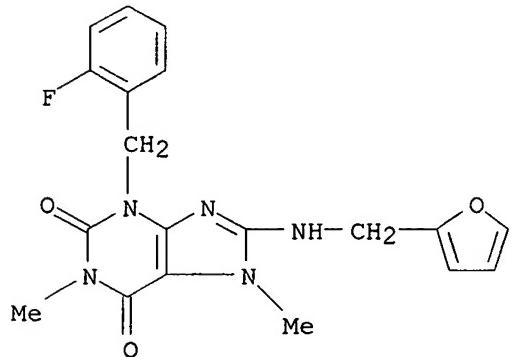
CN 1H-Purine-2,6-dione, 3-[(2-fluorophenyl)methyl]-8-[(2-furanyl methyl)amino]-3,7-dihydro-1,7-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H18 F N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 27 OF 177 REGISTRY COPYRIGHT 2002 ACS

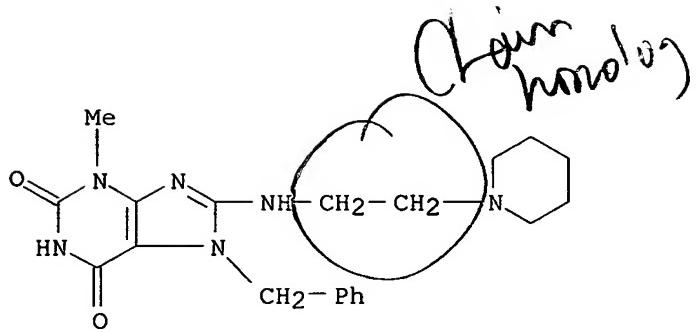
RN 400741-78-8 REGISTRY

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-7-(phenylmethyl)-8-[(2-(1-piperidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H26 N6 O2

SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 28 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 384361-36-8 REGISTRY

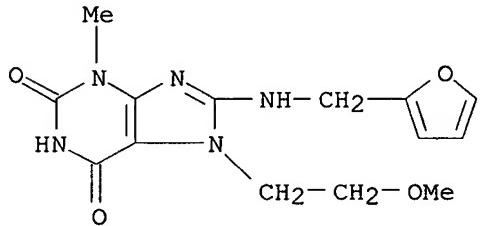
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-7-(2-methoxyethyl)-3-methyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C14 H17 N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 29 OF 177 REGISTRY COPYRIGHT 2002 ACS

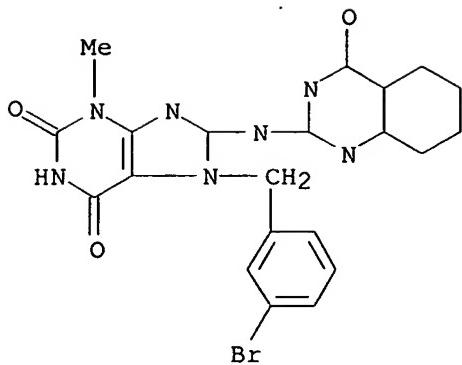
RN 383405-81-0 REGISTRY

CN 1H-Purine-2,6-dione, 7-[(3-bromophenyl)methyl]-8-[(1,4-dihydro-4-oxo-2-quinazolinyl) amino]-3,7-dihydro-3-methyl- (9CI) (CA INDEX NAME)

MF C21 H16 Br N7 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

L29 ANSWER 30 OF 177 REGISTRY COPYRIGHT 2002 ACS

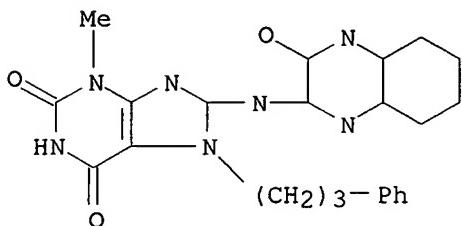
RN 383402-35-5 REGISTRY

CN 1H-Purine-2,6-dione, 8-[(3,4-dihydro-3-oxo-2-quinoxalinyl)amino]-3,7-dihydro-3-methyl-7-(3-phenylpropyl)- (9CI) (CA INDEX NAME)

MF C23 H21 N7 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

L29 ANSWER 31 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 382620-36-2 REGISTRY

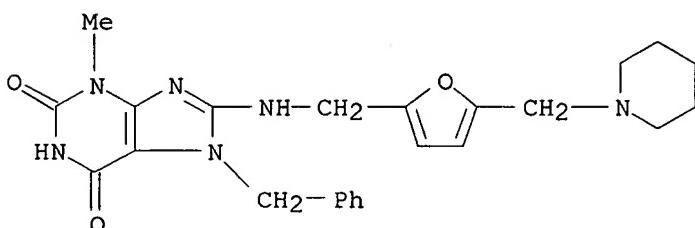
CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-7-(phenylmethyl)-8-[[5-(1-piperidinylmethyl)-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C24 H28 N6 O3

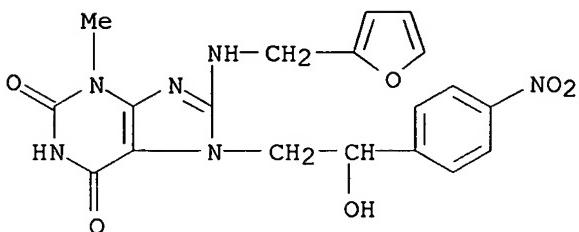
SR Chemical Library

LC STN Files: CHEMCATS



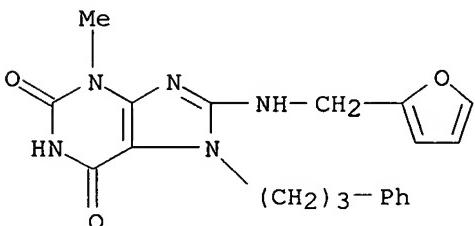
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 32 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 382619-91-2 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-7-[2-hydroxy-2-(4-nitrophenyl)ethyl]-3-methyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 N6 O6  
SR Chemical Library  
LC STN Files: CHEMCATS



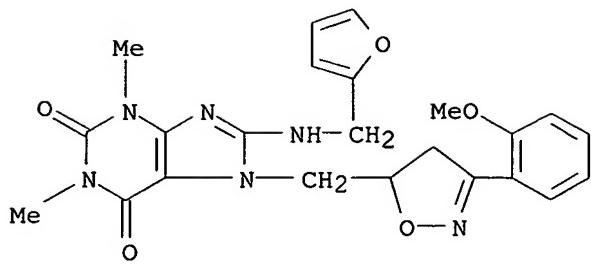
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 33 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 377055-77-1 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-3-methyl-7-(3-phenylpropyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H21 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



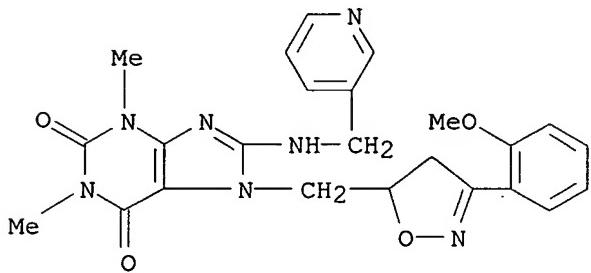
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 34 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 374601-15-7 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[[4,5-dihydro-3-(2-methoxyphenyl)-5-isoxazolyl]methyl]-8-[(2-furanyl methyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C23 H24 N6 O5  
SR Chemical Library  
LC STN Files: CHEMCATS



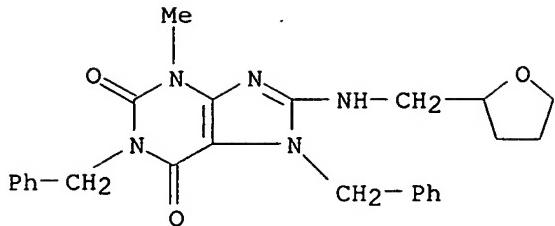
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 35 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 373373-53-6 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(4,5-dihydro-3-(2-methoxyphenyl)-5-isoxazolyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(3-pyridinylmethyl)amino]-(9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C24 H25 N7 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 36 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 372508-79-7 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1,7-bis(phenylmethyl)-8-[(tetrahydro-2-furanyl)methyl]amino]-(9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C25 H27 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 37 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 372500-30-6 REGISTRY

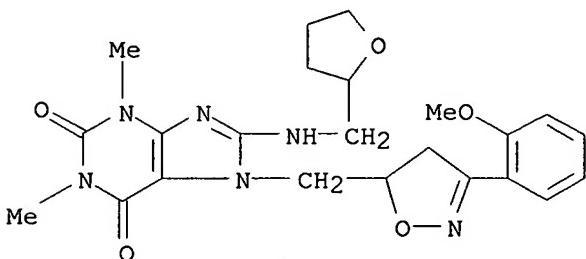
CN 1H-Purine-2,6-dione, 7-[[4,5-dihydro-3-(2-methoxyphenyl)-5-isoxazolyl]methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C23 H28 N6 O5

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 38 OF 177 REGISTRY COPYRIGHT 2002 ACS

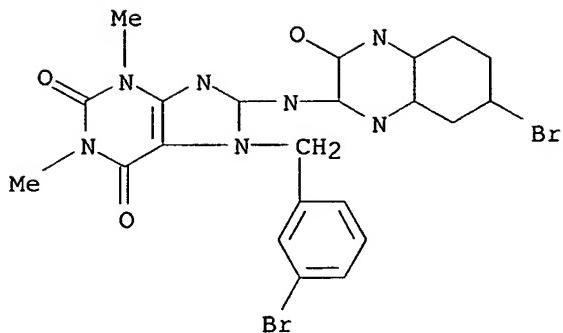
RN 372088-39-6 REGISTRY

CN 1H-Purine-2,6-dione, 8-[(7-bromo-3,4-dihydro-3-oxo-2-quinoxalinyl)amino]-7-[(3-bromophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

MF C22 H17 Br2 N7 O3

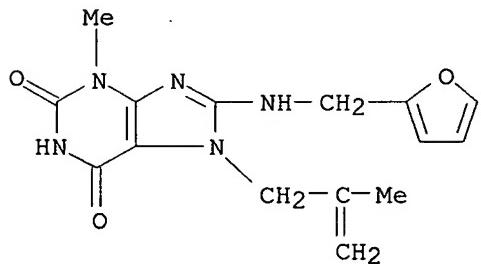
SR Chemical Library

LC STN Files: CHEMCATS



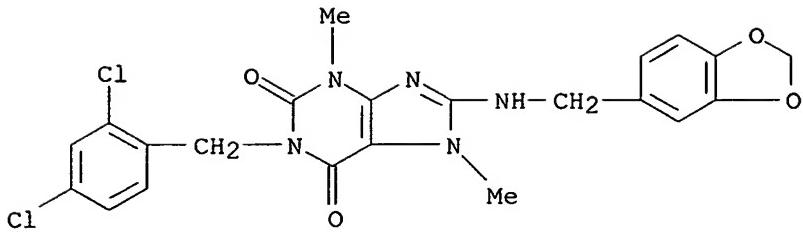
\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

L29 ANSWER 39 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 371213-98-8 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-3-methyl-7-(2-methyl-2-propenyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C15 H17 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 40 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 370075-35-7 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-1-[(2,4-dichlorophenyl)methyl]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H19 Cl2 N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 41 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 369607-22-7 REGISTRY

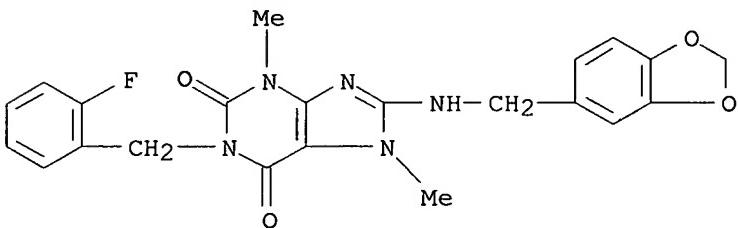
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-1-[(2-fluorophenyl)methyl]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H20 F N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 42 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 369606-77-9 REGISTRY

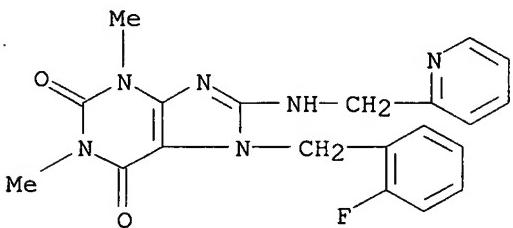
CN 1H-Purine-2,6-dione, 7-[(2-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H19 F N6 O2

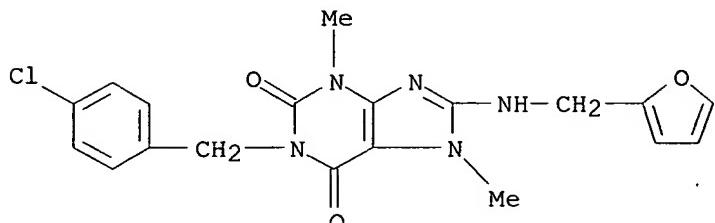
SR Chemical Library

LC STN Files: CHEMCATS



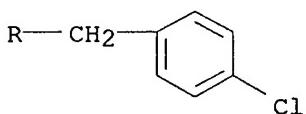
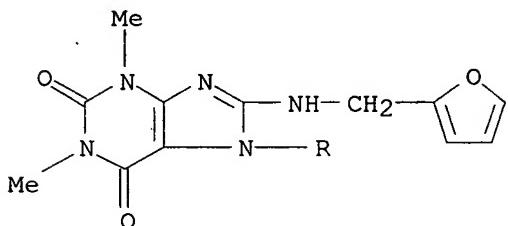
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 43 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 369606-39-3 REGISTRY  
CN 1H-Purine-2,6-dione, 1-[(4-chlorophenyl)methyl]-8-[(2-furanylmethyl)amino]-  
3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 Cl N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

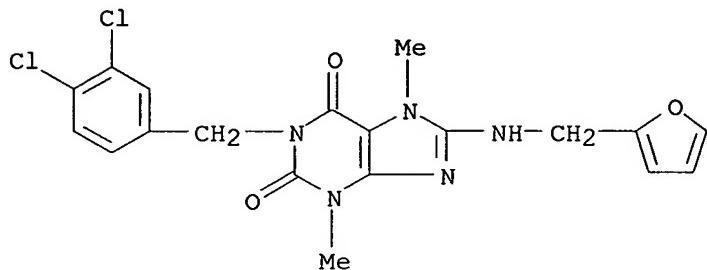
L29 ANSWER 44 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 368841-22-9 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(4-chlorophenyl)methyl]-8-[(2-furanylmethyl)amino]-  
3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 Cl N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

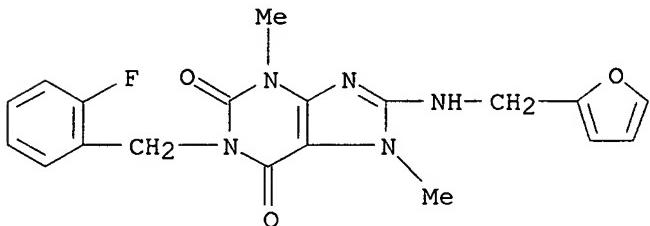
L29 ANSWER 45 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 368838-10-2 REGISTRY

CN 1H-Purine-2,6-dione, 1-[(3,4-dichlorophenyl)methyl]-8-[(2-furanyl methyl)amino]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C19 H17 Cl2 N5 O3  
 SR Chemical Library  
 LC STN Files: CHEMCATS



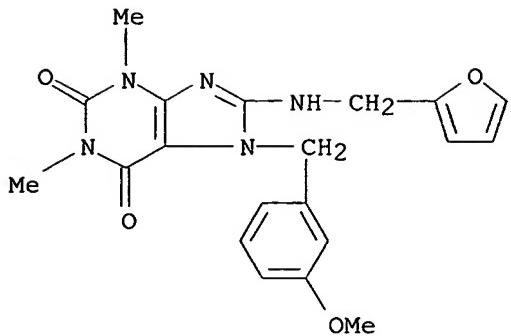
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 46 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 368837-92-7 REGISTRY  
 CN 1H-Purine-2,6-dione, 1-[(2-fluorophenyl)methyl]-8-[(2-furanyl methyl)amino]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C19 H18 F N5 O3  
 SR Chemical Library  
 LC STN Files: CHEMCATS



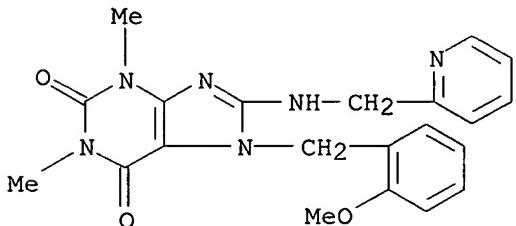
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 47 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 364746-35-0 REGISTRY  
 CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-7-[(3-methoxyphenyl)methyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C20 H21 N5 O4  
 SR Chemical Library  
 LC STN Files: CHEMCATS



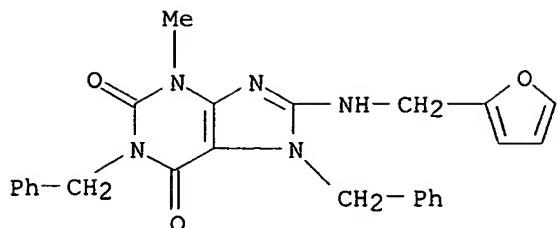
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 48 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 364746-13-4 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[(2-methoxyphenyl)methyl]-1,3-dimethyl-8-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C21 H22 N6 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 49 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 364741-15-1 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-3-methyl-1,7-bis(phenylmethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C25 H23 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 50 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 364739-63-9 REGISTRY

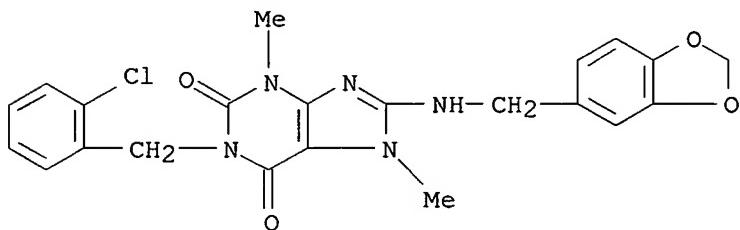
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-1-[(2-chlorophenyl)methyl]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H20 Cl N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 51 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 364619-61-4 REGISTRY

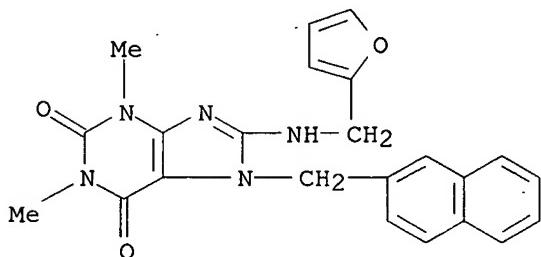
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-1,3-dimethyl-7-(2-naphthalenylmethyl)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C23 H21 N5 O3

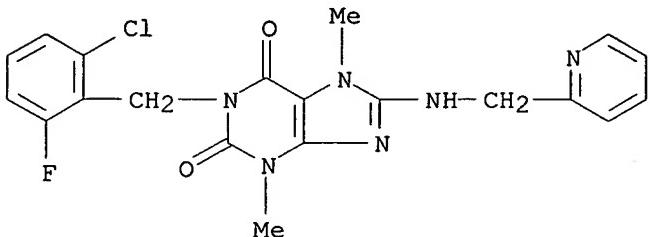
SR Chemical Library

LC STN Files: CHEMCATS



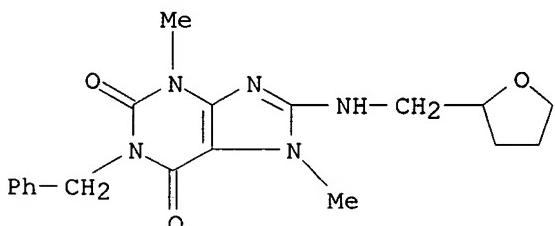
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 52 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 364595-00-6 REGISTRY  
CN 1H-Purine-2,6-dione, 1-[(2-chloro-6-fluorophenyl)methyl]-3,7-dihydro-3,7-dimethyl-8-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H18 Cl F N6 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



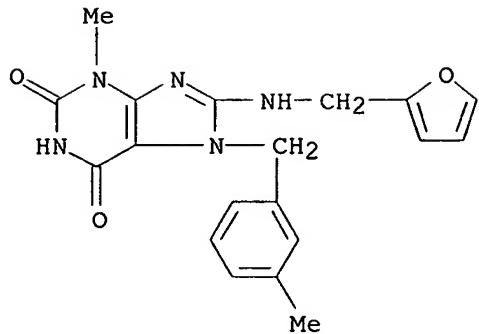
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 53 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 364382-81-0 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(phenylmethyl)-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H23 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



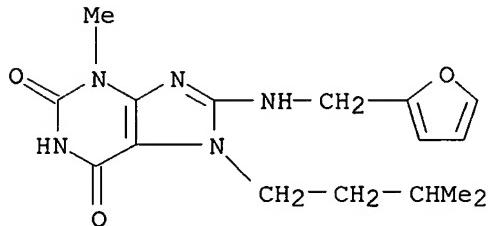
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 54 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 361174-87-0 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-3-methyl-7-[(3-methylphenyl)methyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H19 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



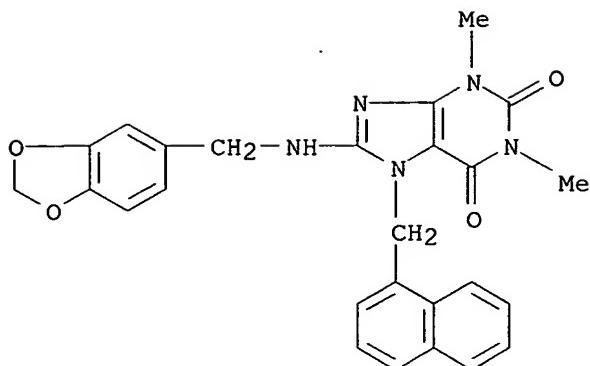
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 55 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 361174-86-9 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-3-methyl-7-(3-methylbutyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C16 H21 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



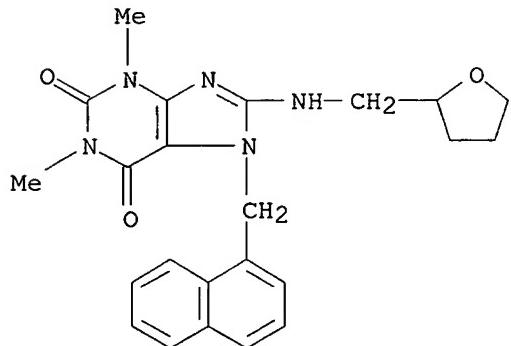
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 56 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359910-42-2 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl) amino]-3,7-dihydro-1,3-dimethyl-7-(1-naphthalenylmethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C26 H23 N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



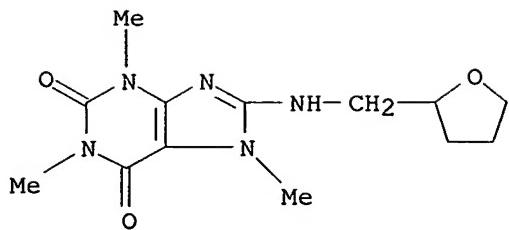
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 57 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359910-16-0 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(1-naphthalenylmethyl)-8-  
[[ (tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C23 H25 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



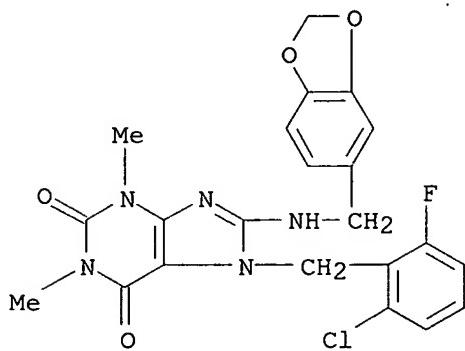
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 58 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359909-89-0 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(tetrahydro-2-  
furanyl)methyl]amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C13 H19 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



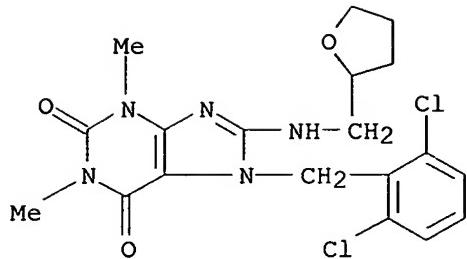
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 59 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359909-79-8 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(2-chloro-6-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H19 Cl F N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



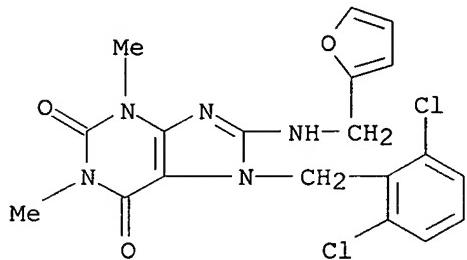
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 60 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359909-15-2 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2,6-dichlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H21 Cl2 N5 O3  
SR Chemical Library



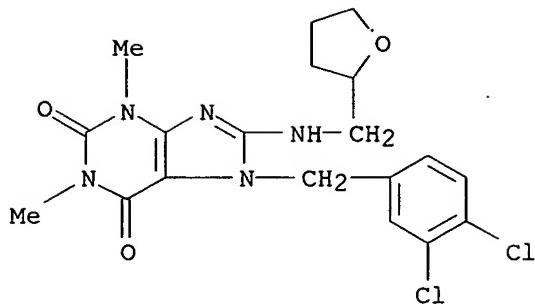
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 61 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359909-13-0 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2,6-dichlorophenyl)methyl]-8-[(2-furanyl)methyl]amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H17 Cl2 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



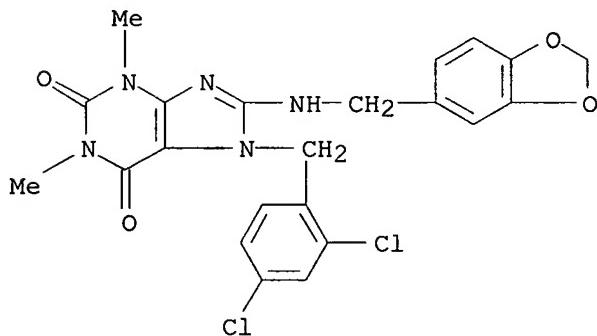
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 62 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359908-80-8 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(3,4-dichlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H21 Cl2 N5 O3  
SR Chemical Library



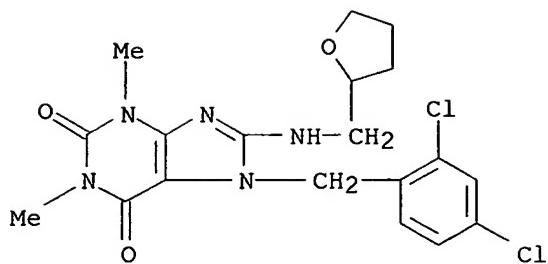
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 63 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359908-48-8 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(2,4-dichlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H19 Cl2 N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



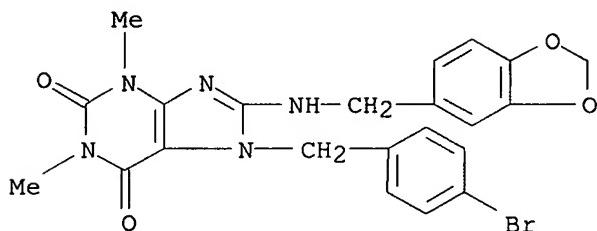
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 64 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359908-24-0 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2,4-dichlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H21 Cl2 N5 O3  
SR Chemical Library



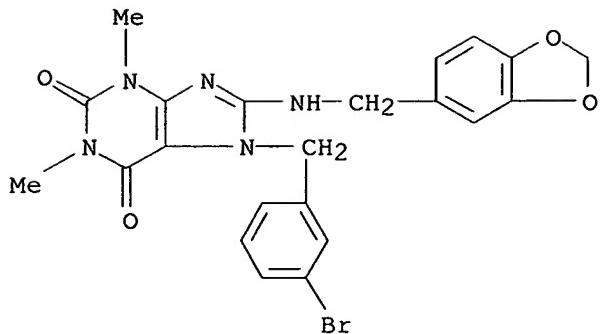
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 65 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359907-97-4 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(4-bromophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H20 Br N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 66 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359907-72-5 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(3-bromophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H20 Br N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 67 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359907-54-3 REGISTRY

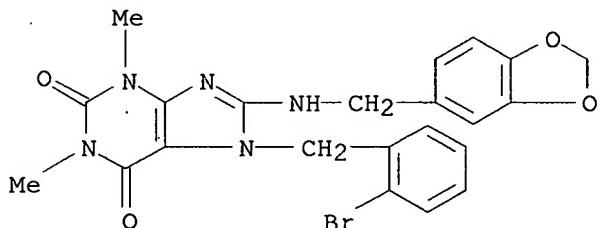
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(2-bromophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H20 Br N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 68 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359907-30-5 REGISTRY

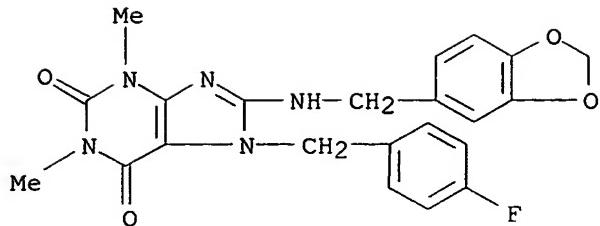
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(4-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H20 F N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 69 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359907-14-5 REGISTRY

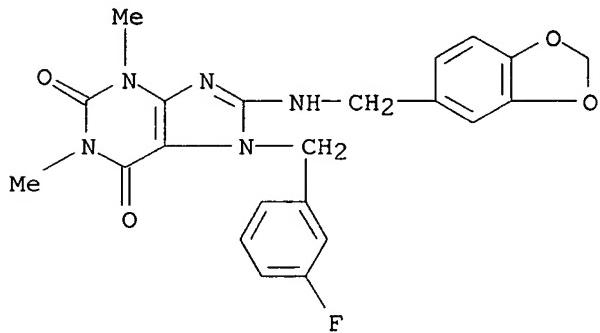
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(3-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H20 F N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 70 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359906-89-1 REGISTRY

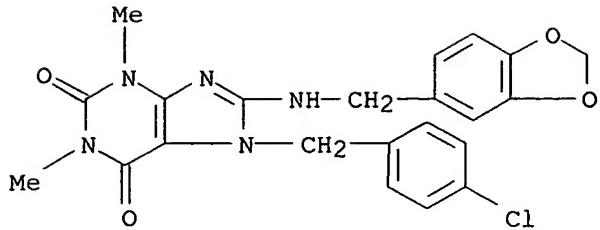
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(4-chlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H20 Cl N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 71 OF 177 REGISTRY COPYRIGHT 2002 ACS

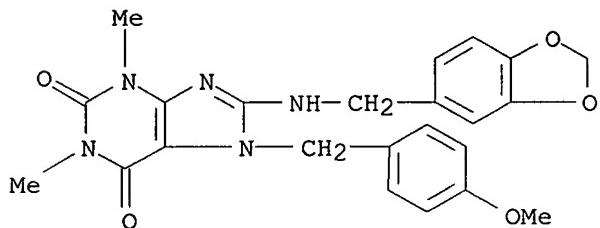
RN 359906-39-1 REGISTRY

CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-3,7-dihydro-7-[(4-methoxyphenyl)methyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C23 H23 N5 O5

SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 72 OF 177 REGISTRY COPYRIGHT 2002 ACS

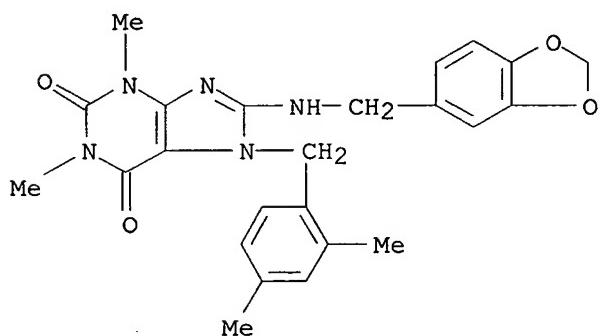
RN 359906-21-1 REGISTRY

CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(2,4-dimethylphenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

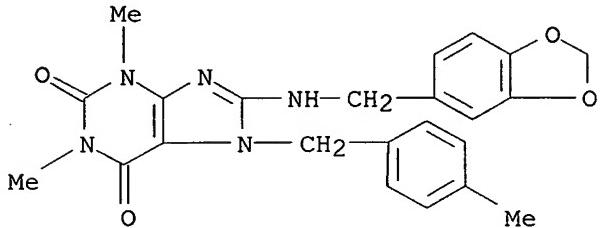
MF C24 H25 N5 O4

SR Chemical Library



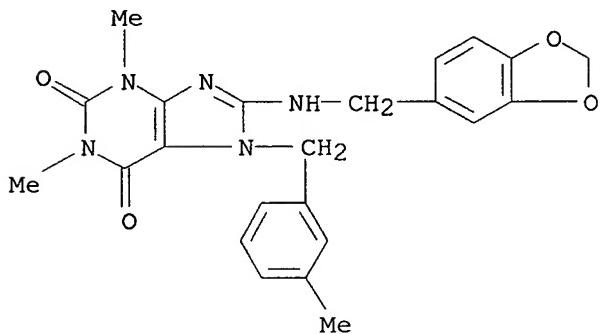
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 73 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359906-04-0 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-3,7-dihydro-1,3-dimethyl-7-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C23 H23 N5 O4  
SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

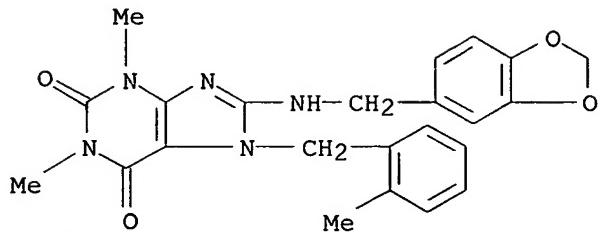
L29 ANSWER 74 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359905-89-8 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-3,7-dihydro-1,3-dimethyl-7-[(3-methylphenyl)methyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C23 H23 N5 O4  
SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

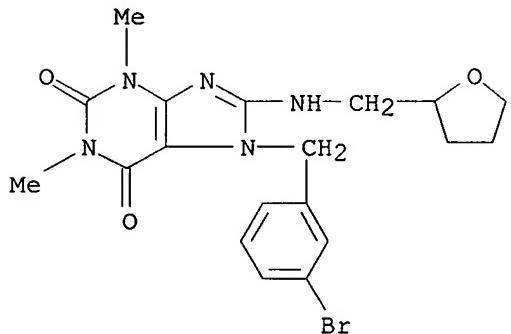
L29 ANSWER 75 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359905-68-3 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-3,7-dihydro-1,3-dimethyl-7-[(2-methylphenyl)methyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD

MF C23 H23 N5 O4  
SR Chemical Library



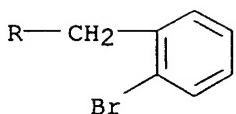
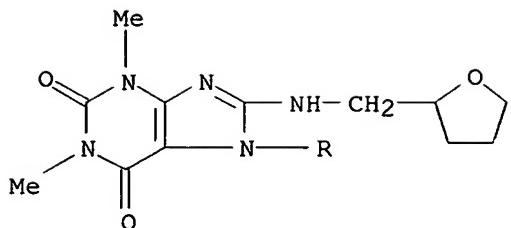
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 76 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359905-22-9 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(3-bromophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H22 Br N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 77 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359904-85-1 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2-bromophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H22 Br N5 O3  
SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 78 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359904-82-8 REGISTRY

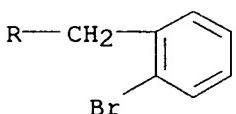
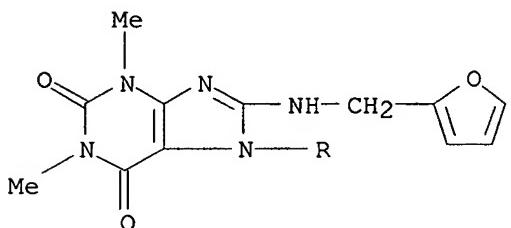
CN 1H-Purine-2,6-dione, 7-[(2-bromophenyl)methyl]-8-[(2-furanylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H18 Br N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 79 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359904-33-9 REGISTRY

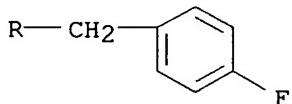
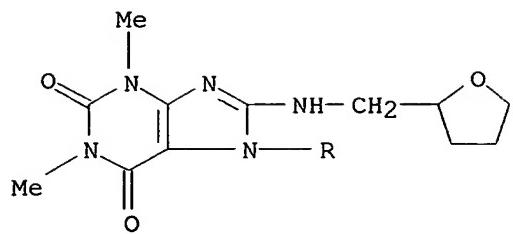
CN 1H-Purine-2,6-dione, 7-[(4-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanylmethyl)amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H22 F N5 O3

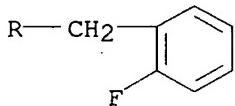
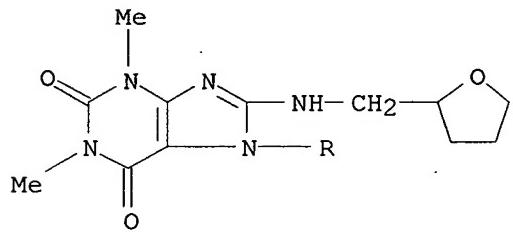
SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 80 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359903-69-8 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-  
[[ (tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H22 F N5 O3  
SR Chemical Library

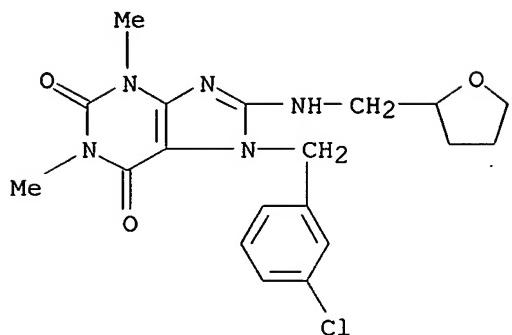


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 81 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359903-06-3 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(3-chlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-  
[[ (tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H22 Cl N5 O3

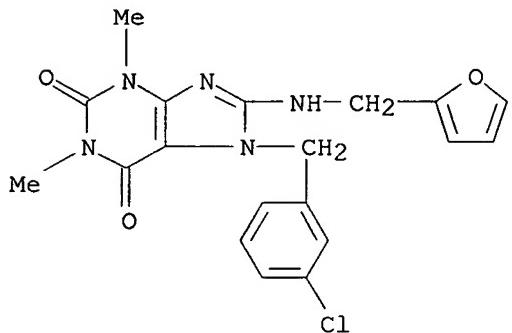
Searched by: Mary Hale 308-4258 CM-1 1E01

SR Chemical Library



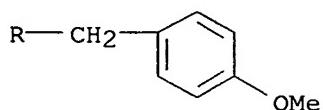
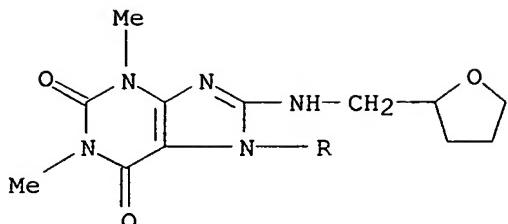
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 82 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359903-03-0 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(3-chlorophenyl)methyl]-8-[(2-furanyl methyl)amino]-  
3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 Cl N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 83 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359902-60-6 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[(4-methoxyphenyl)methyl]-1,3-dimethyl-  
8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H25 N5 O4  
SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 84 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359902-58-2 REGISTRY

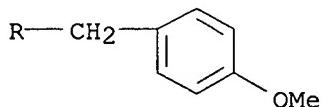
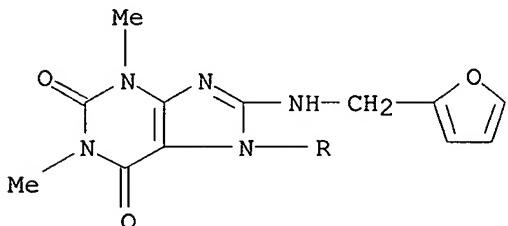
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-7-[(4-methoxyphenyl)methyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H21 N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 85 OF 177 REGISTRY COPYRIGHT 2002 ACS

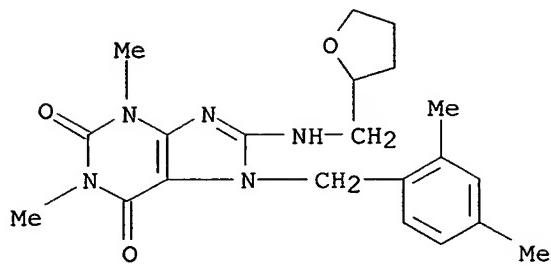
RN 359902-26-4 REGISTRY

CN 1H-Purine-2,6-dione, 7-[(2,4-dimethylphenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C21 H27 N5 O3

SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 86 OF 177 REGISTRY COPYRIGHT 2002 ACS

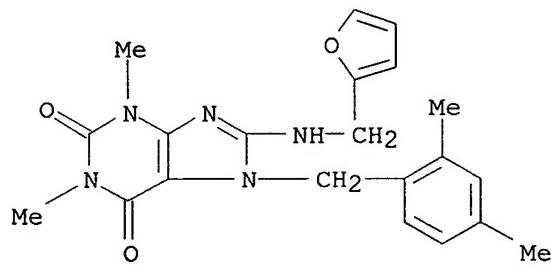
RN 359902-24-2 REGISTRY

CN 1H-Purine-2,6-dione, 7-[(2,4-dimethylphenyl)methyl]-8-[(2-furanyl methyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C21 H23 N5 O3

SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 87 OF 177 REGISTRY COPYRIGHT 2002 ACS

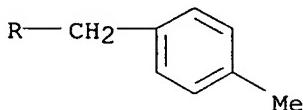
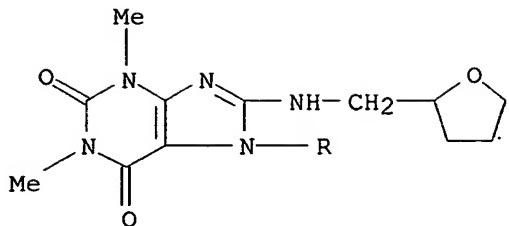
RN 359902-02-6 REGISTRY

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[(4-methylphenyl)methyl]-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H25 N5 O3

SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 88 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359902-00-4 REGISTRY

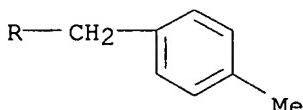
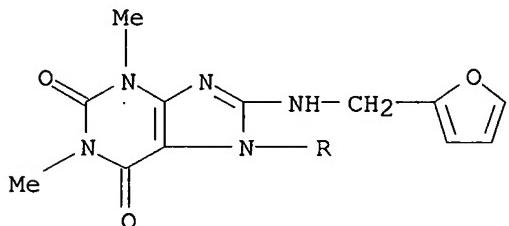
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-1,3-dimethyl-7-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H21 N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 89 OF 177 REGISTRY COPYRIGHT 2002 ACS

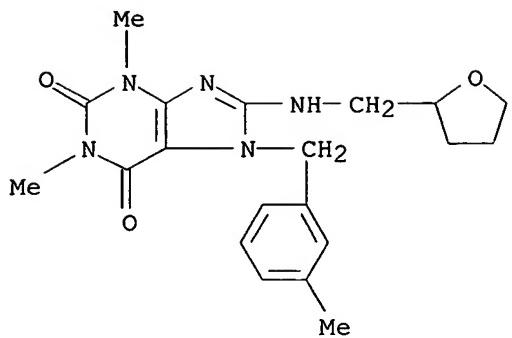
RN 359901-72-7 REGISTRY

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[(3-methylphenyl)methyl]-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H25 N5 O3

SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 90 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 359901-71-6 REGISTRY

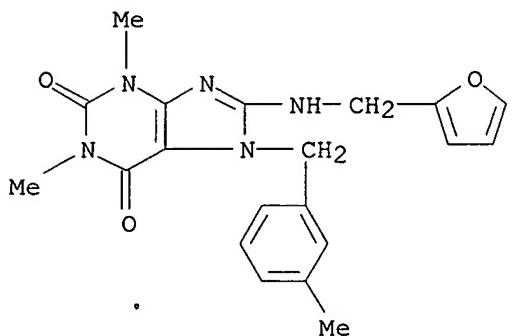
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-1,3-dimethyl-7-[(3-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H21 N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 91 OF 177 REGISTRY COPYRIGHT 2002 ACS

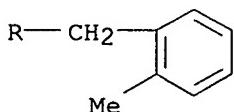
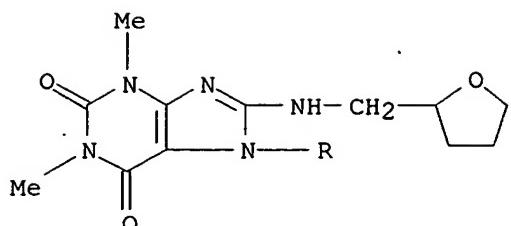
RN 359698-19-4 REGISTRY

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-[(2-methylphenyl)methyl]-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)

FS 3D CONCORD

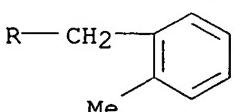
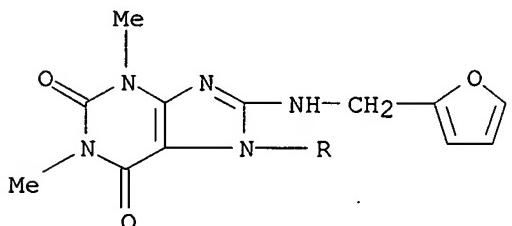
MF C20 H25 N5 O3

SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

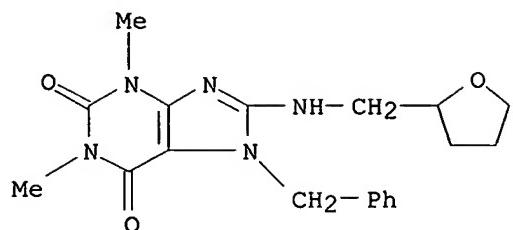
L29 ANSWER 92 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359698-17-2 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-1,3-dimethyl-7-[(2-methylphenyl)methyl] - (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H21 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

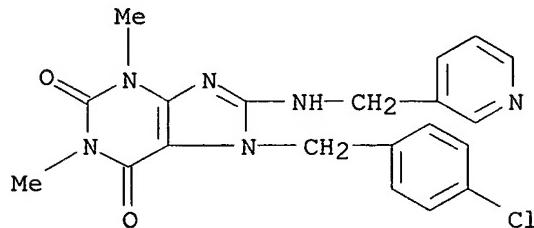
L29 ANSWER 93 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 359697-84-0 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)-8-[(tetrahydro-2-furanyl methyl) amino] - (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H23 N5 O3  
SR Chemical Library

LC STN Files: CHEMCATS



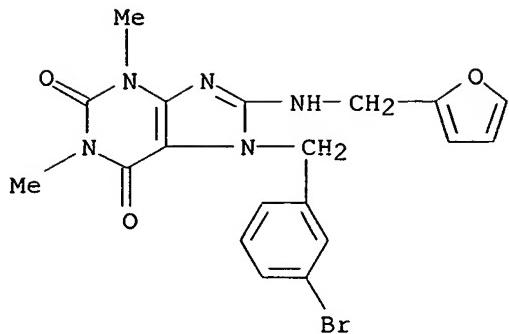
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 94 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 354132-96-0 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(4-chlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H19 Cl N6 O2  
SR Chemical Library



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 95 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 353763-12-9 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(3-bromophenyl)methyl]-8-[(2-furanylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 Br N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 96 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 353507-11-6 REGISTRY

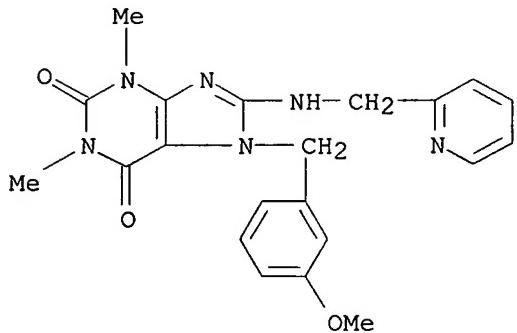
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[(3-methoxyphenyl)methyl]-1,3-dimethyl-8-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C21 H22 N6 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 97 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 333752-36-6 REGISTRY

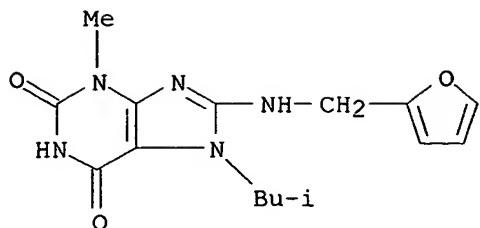
CN 1H-Purine-2,6-dione, 8-[(2-furanylmethyl)amino]-3,7-dihydro-3-methyl-7-(2-methylpropyl)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C15 H19 N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 98 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 333752-30-0 REGISTRY

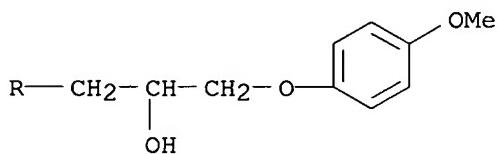
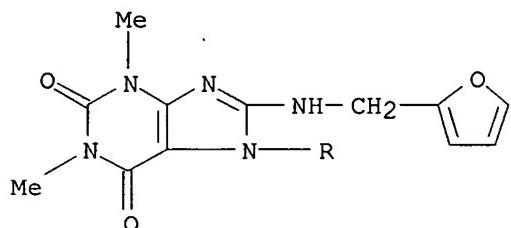
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-7-[2-hydroxy-3-(4-methoxyphenoxy) propyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H25 N5 O6

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 99 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 333752-29-7 REGISTRY

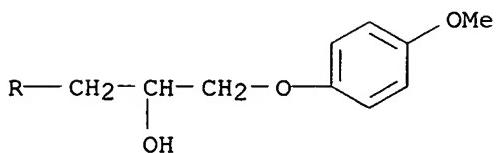
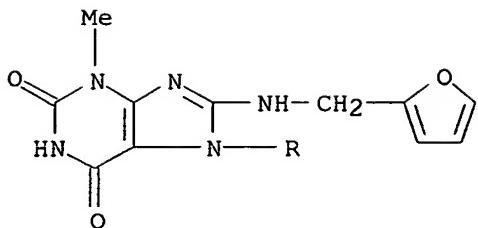
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-7-[2-hydroxy-3-(4-methoxyphenoxy) propyl]-3-methyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C21 H23 N5 O6

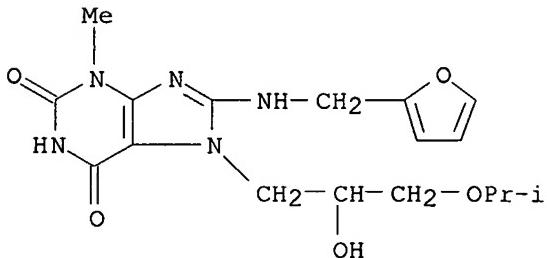
SR Chemical Library

LC STN Files: CHEMCATS



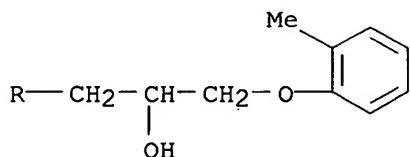
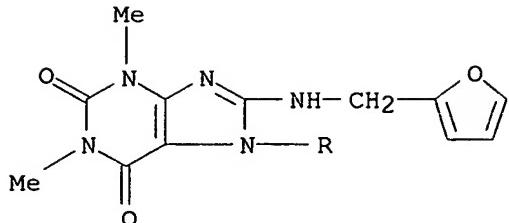
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 100 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 333752-28-6 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-7-[2-hydroxy-3-(1-methylethoxy) propyl]-3-methyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C17 H23 N5 O5  
SR Chemical Library  
LC STN Files: CHEMCATS



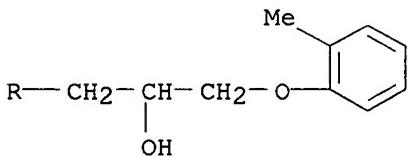
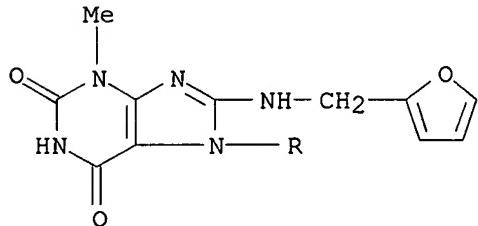
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 101 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 333752-26-4 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-7-[2-hydroxy-3-(2-methylphenoxy) propyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H25 N5 O5  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

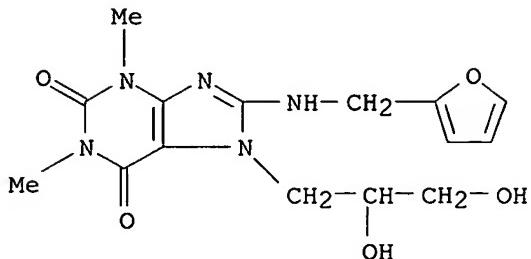
L29 ANSWER 102 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 333752-25-3 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-7-[2-hydroxy-3-(2-methylphenoxy) propyl]-3-methyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C21 H23 N5 O5  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

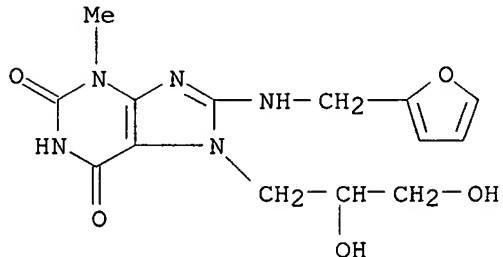
L29 ANSWER 103 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 333752-24-2 REGISTRY  
CN 1H-Purine-2,6-dione, 7-(2,3-dihydroxypropyl)-8-[(2-furanyl methyl) amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD

MF C15 H19 N5 O5  
SR Chemical Library  
LC STN Files: CHEMCATS



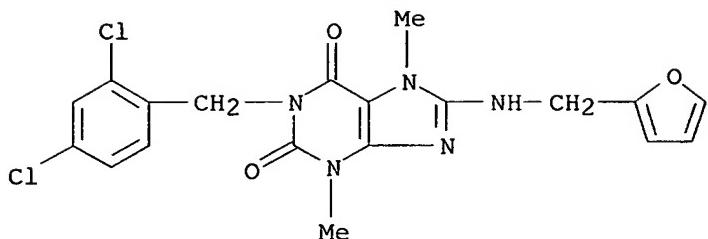
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 104 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 333752-23-1 REGISTRY  
CN 1H-Purine-2,6-dione, 7-(2,3-dihydroxypropyl)-8-[(2-furanylmethyl)amino]-3,7-dihydro-3-methyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C14 H17 N5 O5  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 105 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 332102-07-5 REGISTRY  
CN 1H-Purine-2,6-dione, 1-[(2,4-dichlorophenyl)methyl]-8-[(2-furanylmethyl)amino]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H17 Cl2 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 106 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 330829-17-9 REGISTRY

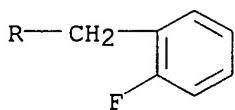
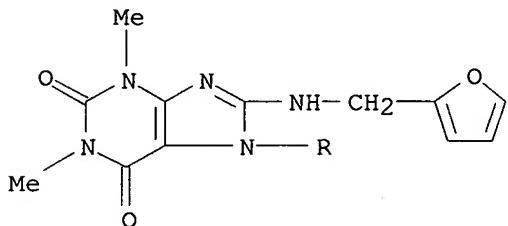
CN 1H-Purine-2,6-dione, 7-[(2-fluorophenyl)methyl]-8-[(2-furanyl methyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H18 F N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 107 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 330827-80-0 REGISTRY

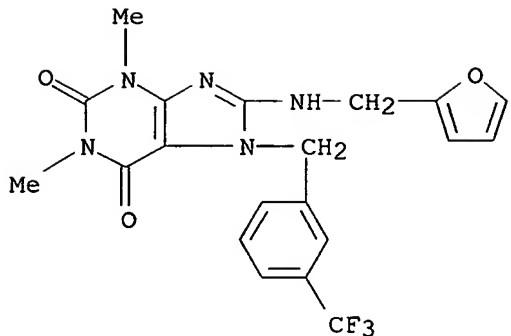
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-1,3-dimethyl-7-[[3-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H18 F3 N5 O3

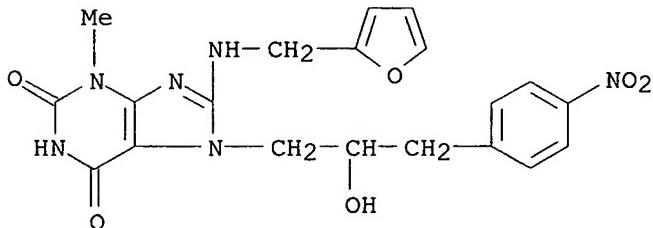
SR Chemical Library

LC STN Files: CHEMCATS



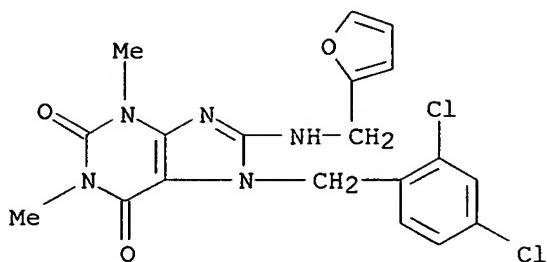
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 108 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 329702-45-6 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-7-[2-hydroxy-3-(4-nitrophenyl)propyl]-3-methyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H20 N6 O6  
SR Chemical Library  
LC STN Files: CHEMCATS



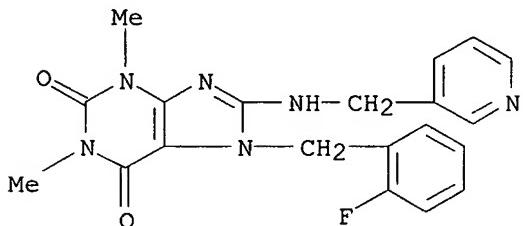
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 109 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 327101-36-0 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2,4-dichlorophenyl)methyl]-8-[(2-furanyl methyl) amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H17 Cl2 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



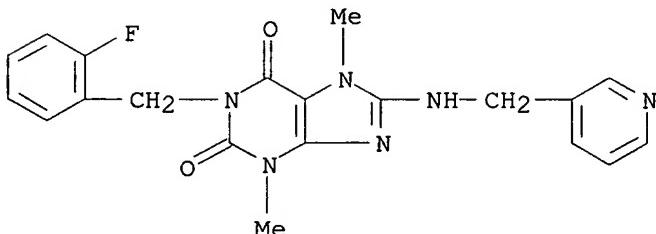
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 110 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 327100-26-5 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H19 F N6 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



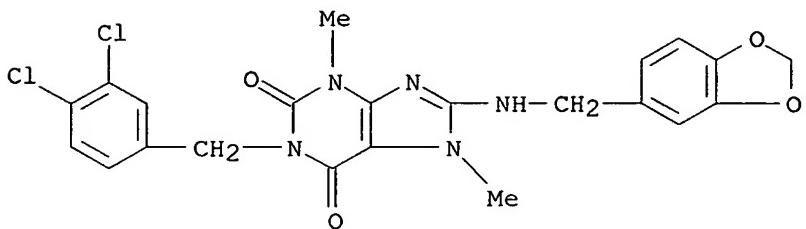
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 111 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 327099-04-7 REGISTRY  
CN 1H-Purine-2,6-dione, 1-[(2-fluorophenyl)methyl]-3,7-dihydro-3,7-dimethyl-8-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H19 F N6 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



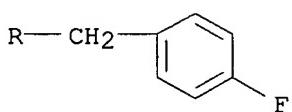
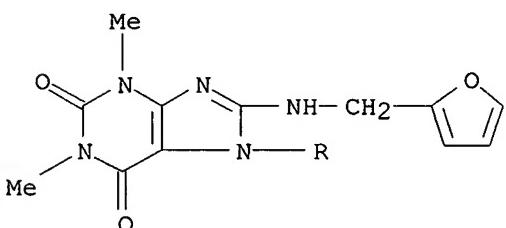
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 112 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 327098-80-6 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-1-[(3,4-dichlorophenyl)methyl]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H19 Cl2 N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 113 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 327097-91-6 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(4-fluorophenyl)methyl]-8-[(2-furanylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 F N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS

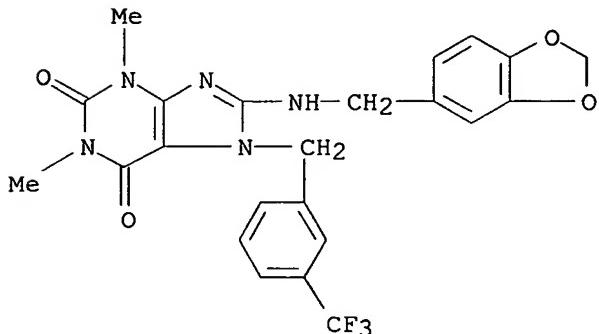


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 114 OF 177 REGISTRY COPYRIGHT 2002 ACS

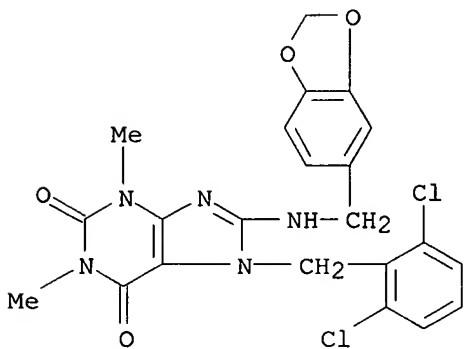
Searched by: Mary Hale 308-4258 CM-1 1E01

RN 317843-50-8 REGISTRY  
 CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-3,7-dihydro-1,3-dimethyl-7-[(3-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C23 H20 F3 N5 O4  
 SR Chemical Library  
 LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

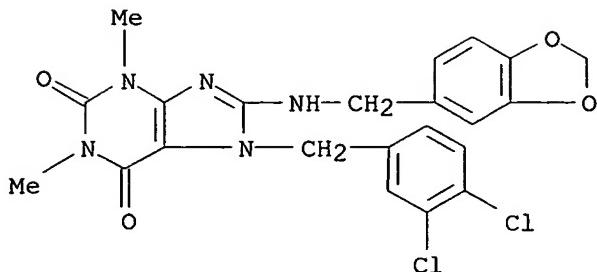
L29 ANSWER 115 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 317843-20-2 REGISTRY  
 CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(2,6-dichlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C22 H19 Cl2 N5 O4  
 SR Chemical Library  
 LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

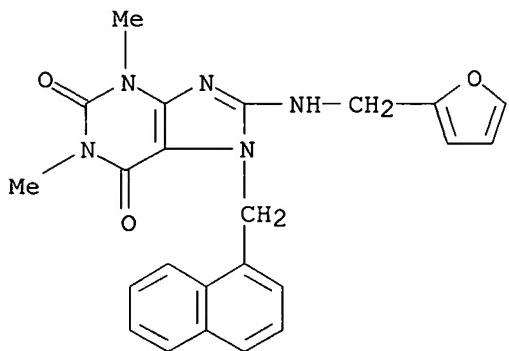
L29 ANSWER 116 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 317841-58-0 REGISTRY  
 CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(3,4-dichlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD

MF C22 H19 Cl2 N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



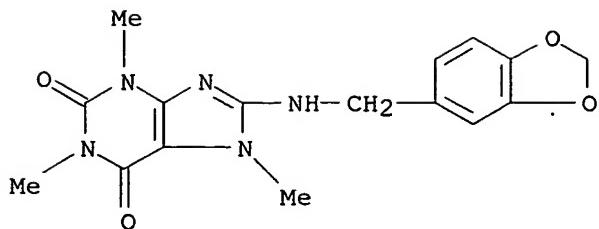
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 117 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 309938-21-4 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-1,3-dimethyl-7-(1-naphthalenylmethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C23 H21 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



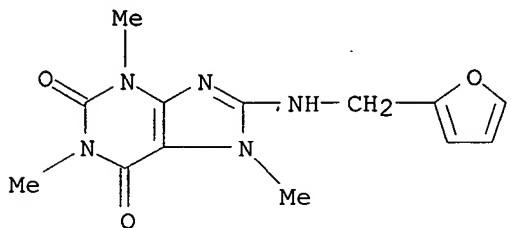
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 118 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 309938-15-6 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl) amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C16 H17 N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



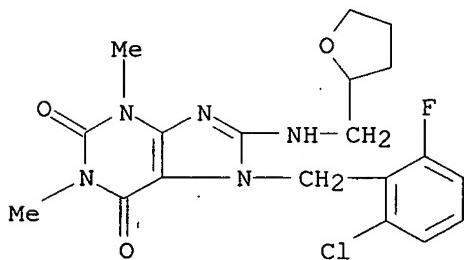
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 119 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 309938-12-3 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C13 H15 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



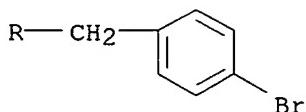
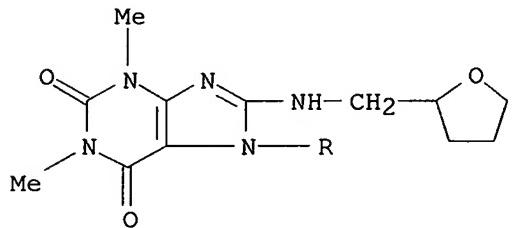
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 120 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 309938-04-3 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2-chloro-6-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H21 Cl F N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



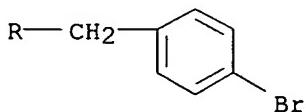
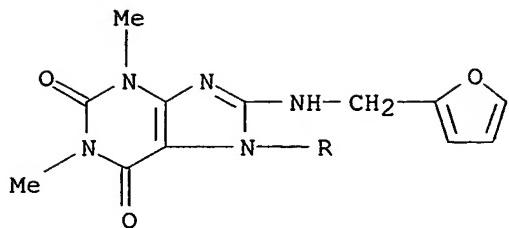
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 121 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 309937-89-1 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(4-bromophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-  
[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H22 Br N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 122 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 309937-88-0 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(4-bromophenyl)methyl]-8-[(2-furanylmethyl)amino]-  
3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 Br N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 123 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 309937-49-3 REGISTRY

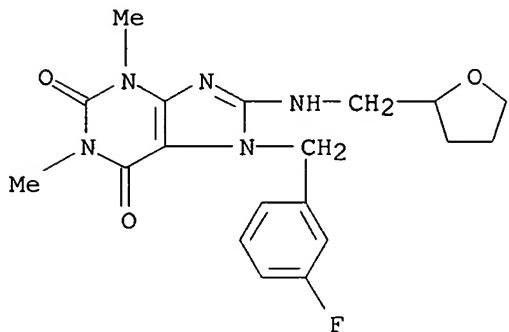
CN 1H-Purine-2,6-dione, 7-[(3-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-[(tetrahydro-2-furanyl)methyl]amino- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H22 F N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 124 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 309937-47-1 REGISTRY

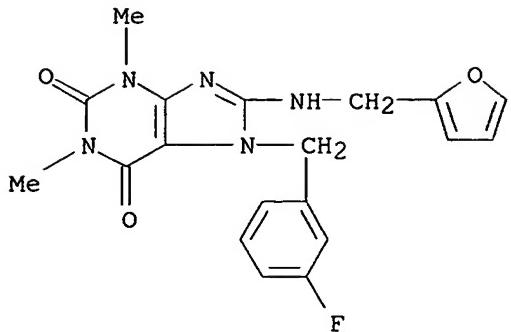
CN 1H-Purine-2,6-dione, 7-[(3-fluorophenyl)methyl]-8-[(2-furanyl)methyl]amino-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H18 F N5 O3

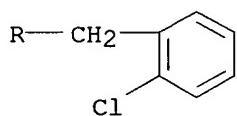
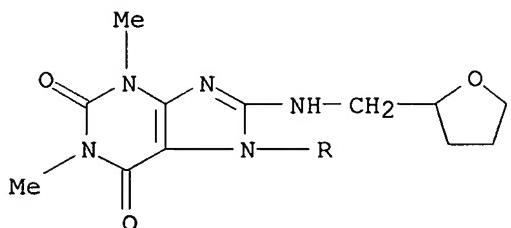
SR Chemical Library

LC STN Files: CHEMCATS



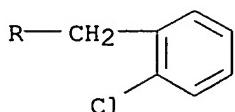
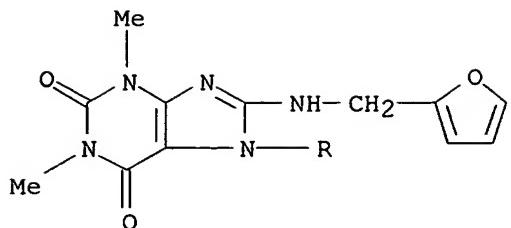
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 125 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 309937-31-3 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2-chlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl-8-  
[[ (tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H22 Cl N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



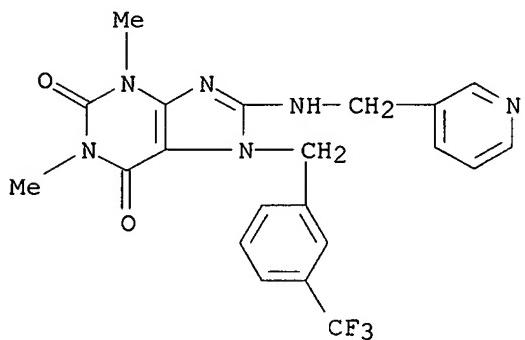
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 126 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 309937-29-9 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2-chlorophenyl)methyl]-8-[(2-furanyl)methyl]amino]-  
3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H18 Cl N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



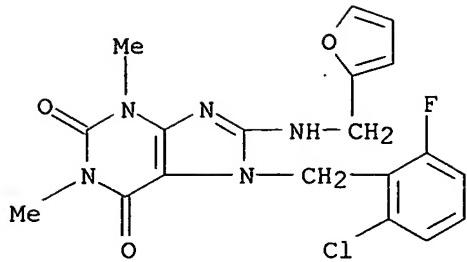
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 127 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 305866-33-5 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(3-pyridinylmethyl)amino]-7-[[3-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C21 H19 F3 N6 O2  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 128 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 305865-20-7 REGISTRY  
CN 1H-Purine-2,6-dione, 7-[(2-chloro-6-fluorophenyl)methyl]-8-[(2-furanylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H17 Cl F N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 129 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 305864-73-7 REGISTRY

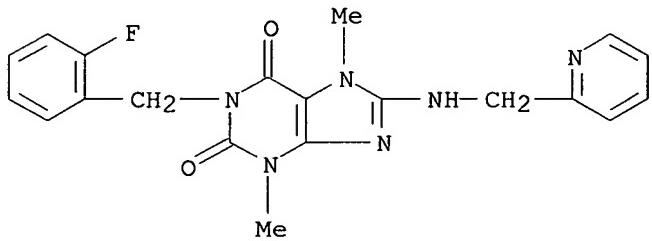
CN 1H-Purine-2,6-dione, 1-[(2-fluorophenyl)methyl]-3,7-dihydro-3,7-dimethyl-8-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H19 F N6 O2

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 130 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 305863-82-5 REGISTRY

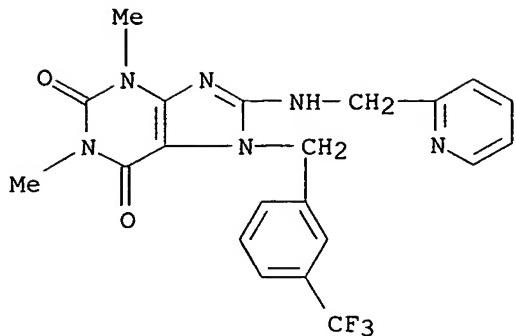
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(2-pyridinylmethyl)amino]-7-[[3-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C21 H19 F3 N6 O2

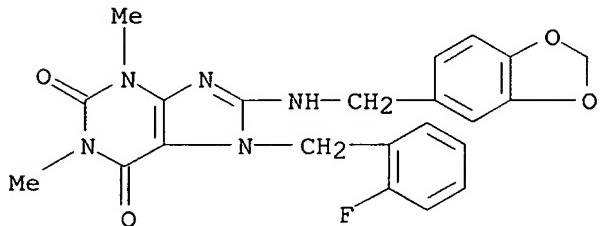
SR Chemical Library

LC STN Files: CHEMCATS



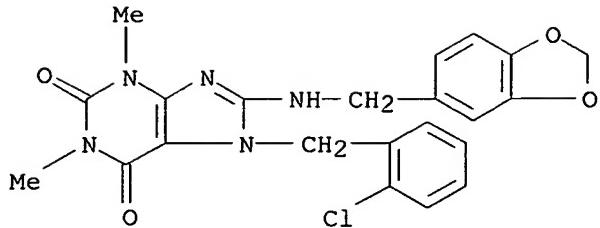
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 131 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 305863-03-0 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(2-fluorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H20 F N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 132 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 304880-66-8 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-7-[(2-chlorophenyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H20 Cl N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 133 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 304879-74-1 REGISTRY

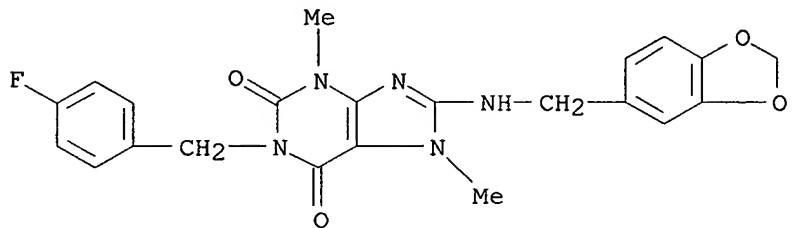
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-1-[(4-fluorophenyl)methyl]-3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C22 H20 F N5 O4

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 134 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 304878-84-0 REGISTRY

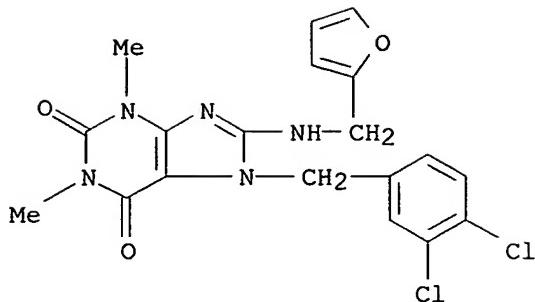
CN 1H-Purine-2,6-dione, 7-[(3,4-dichlorophenyl)methyl]-8-[(2-furanyl)methyl]amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H17 Cl2 N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 135 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 302799-23-1 REGISTRY

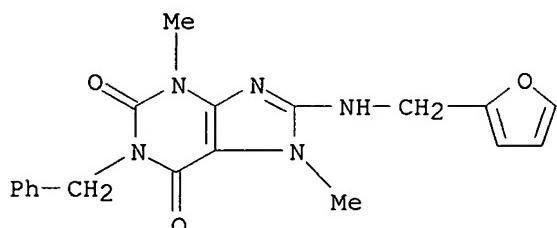
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-3,7-dimethyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H19 N5 O3

SR Chemical Library

LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 136 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 302796-84-5 REGISTRY

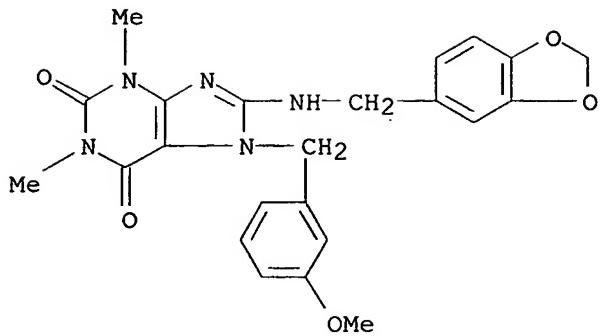
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl) amino]-3,7-dihydro-7-[(3-methoxyphenyl)methyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C23 H23 N5 O5

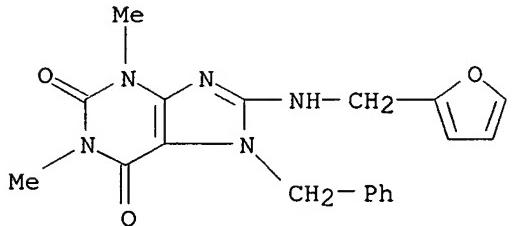
SR Chemical Library

LC STN Files: CHEMCATS



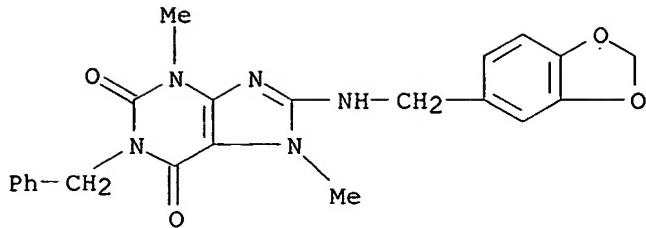
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 137 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 300701-50-2 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl) amino]-3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H19 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



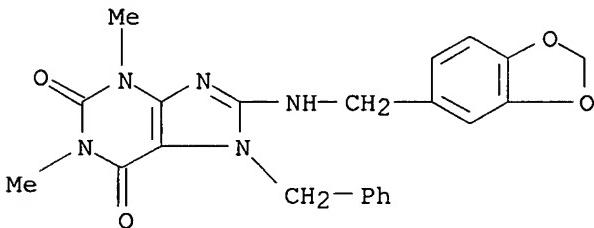
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 138 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 300589-32-6 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl) amino]-3,7-dihydro-3,7-dimethyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H21 N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



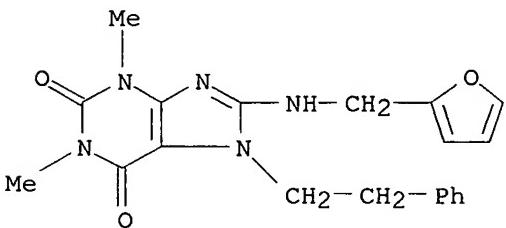
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 139 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 300587-98-8 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)amino]-3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H21 N5 O4  
SR Chemical Library  
LC STN Files: CHEMCATS



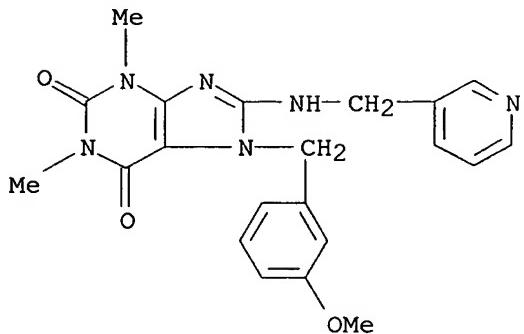
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 140 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 300586-94-1 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-1,3-dimethyl-7-(2-phenylethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H21 N5 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



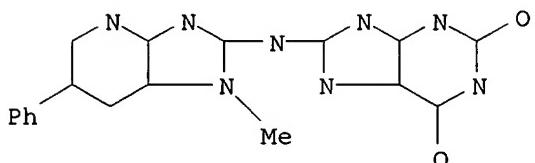
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 141 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 300586-55-4 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-7-[(3-methoxyphenyl)methyl]-1,3-dimethyl-  
8-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C21 H22 N6 O3  
SR Chemical Library  
LC STN Files: CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L29 ANSWER 142 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 289914-71-2 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(1-methyl-6-phenyl-1H-imidazo[4,5-b]pyridin-2-yl)amino]- (9CI) (CA INDEX NAME)  
MF C18 H14 N8 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:204054 N-acetyltransferase-dependent activation of 2-hydroxyamino-1-methyl-6-phenylimidazo[4,5-b]pyridine: formation of 2-amino-1-methyl-6-(5-hydroxy)phenylimidazo [4,5-b]pyridine, a possible biomarker for the reactive dose of 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine. Frandsen, Henrik; Alexander, Jan (Institute of Food Safety and Toxicology, Soborg, DK-2860, Den.). Carcinogenesis, 21(6), 1197-1203 (English) 2000. CODEN: CRNGDP. ISSN: 0143-3334. Publisher: Oxford University Press.

AB 2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) is a mutagenic and carcinogenic heterocyclic amine formed during ordinary cooking. PhIP is metabolically activated to the ultimate mutagenic metabolite by CYP P 450-mediated N-hydroxylation followed by phase II esterification. Incubation of N-hydroxy-PhIP (N-OH-PhIP) with cytosol, acetyl CoA (AcCoA) and 2'-deoxyguanosine for 24 h resulted in the formation of three different adducts: N2-(deoxyguanosin-8-yl)-PhIP, N2-(guanosin-8-yl)-PhIP and PhIP-xanthine. One addnl. product, 5-hydroxy-PhIP (5-OH-PhIP), was also identified in the incubation mixts. 5-Hydroxy-PhIP is formed as a degrdn. product of conjugates formed from N-acetoxy-PhIP and protein, glutathione or buffer constituents. A similar spectrum of products was obtained using 3'-phosphoadenosine-5'-phosphosulfate (PAPS) instead of acetyl CoA. Addn. of glutathione (3 mM) to the incubation mixt. resulted in a 50% redn. in both adducts and 5-hydroxy-PhIP formation in liver cytosol. The main product detected was PhIP, suggesting glutathione-dependent redn. of the N-acetoxy-PhIP. Addn. of glutathione to incubation mixts. from the other cytosolic preps. had less dramatic effects. In addn., increasing the amt. of N-OH-PhIP in the incubation mixt. resulted in proportional increased amts. of total adducts and 5-OH-PhIP. Incubation of rat and human S9 with PhIP resulted in the formation of only traces of 5-OH-PhIP. Fortification with AcCoA clearly increased the formation of 5-OH-PhIP. Addn. of the CYP 450 1A2 inhibitor, furafylline, completely inhibited the formation of 5-OH-PhIP in incubations with human S9. These results indicate that both PhIP adducts and 5-OH-PhIP are formed by similar routes of activation of N-OH-PhIP. 5-OH-PhIP may therefore serve as a biomarker for the formation of the ultimate mutagenic metabolite of PhIP. A rat dosed orally with PhIP excreted 1% of the dose as 5-OH-PhIP in the urine at 24 h and 0.05 and 0.01% at 48 and 72 h, resp. This shows that 5-OH-PhIP is also formed in vivo and indicates the possible use of 5-OH-PhIP as a urinary biomarker.

L29 ANSWER 143 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 143410-90-6 REGISTRY

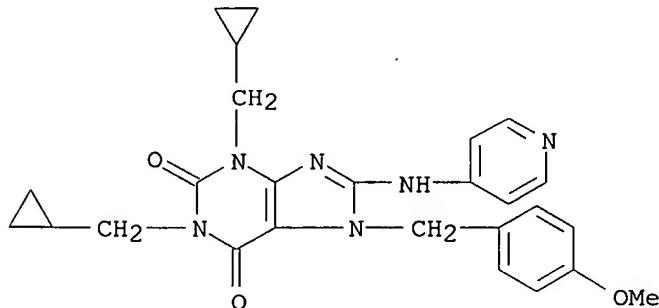
CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-7-[(4-methoxyphenyl)methyl]-8-(4-pyridinylamino)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C26 H28 N6 O3

SR CA

LC STN Files: CA, CAPLUS, CASREACT



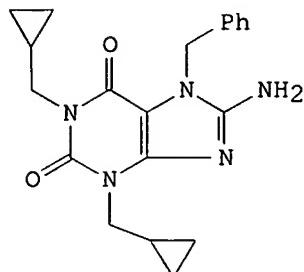
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 117:151010 7-alkyl-8-aminoxanthine and 7-alkyl-8-chloroxanthine derivatives, a method for their preparation and their use as phosphodiesterase inhibitor, antiallergic and for treatment of eosinophilia. Buckle, Derek Richard; Smith, David Glynn; Fenwick, Ashley Edward (Beecham Group PLC, UK). PCT Int. Appl. WO 9205175 A1 19920402, 54 pp. DESIGNATED STATES: W: AU, CA, JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-GB1633 19910923. PRIORITY: GB 1990-20959 19900926.

GI



AB Certain 7-alkylxanthine derivs. (7-alkyl-1H-purine-2,6-diones) are claimed. A process for their prepn. comprises the alkylation of a xanthine deriv. Pharmaceuticals contg. said compds. are claimed for the treatment of disorders assocd. with increased nos. of eosinophils and allergic disorders assocd. with atopy; the compds. are phosphodiesterase inhibitors. These compds. have potential use as inhibitors for tumor necrosis factor, HIV, AIDS, arthritis, and for the treatment of conditions assocd. with infection (no data). Treatment of 8-amino-1,3-bis(cyclopropylmethyl)xanthine with KOCMe<sub>3</sub>/DMF and benzyl bromide gave 8-amino-7-benzyl-1,3-bis(cyclopropylmethyl)xanthine (I) in 84% yield. I was active in the treatment of blood eosinophilia in rats and had activity as phosphodiesterase inhibitor.

L29 ANSWER 144 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 136611-65-9 REGISTRY

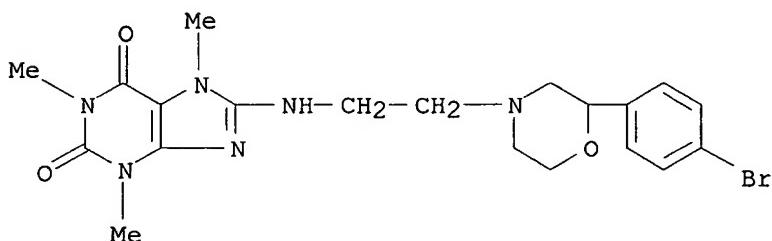
CN 1H-Purine-2,6-dione, 8-[[2-[2-(4-bromophenyl)-4-morpholinyl]ethyl]amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C20 H25 Br N6 O3

SR CA

LC STN Files: CA, CAPLUS, CASREACT



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

Searched by: Mary Hale 308-4258 CM-1 1E01

2 REFERENCES IN FILE CA (1962 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 115:231576 Auxochromic effect of substituents at the 8 position of 1,3,7-trimethylxanthine on the electronic spectra. Iovchev, I.; Zlatkov, A.; Peikov, P.; Gagauzov, I. (MA, Sofia, Bulg.). Farmatsiya (Sofia, Bulgaria), 41(2), 1-5 (Bulgarian) 1991. CODEN: FMTYA2. ISSN: 0428-0296.

AB Basic substituents in the 8 position of caffeine shifted the UV absorption band at 276 nm to 281-294 nm. Strongest effect was noted with N-bound substituents.

REFERENCE 2: 115:182936 Synthesis of (2-aminoethyl)amino derivatives of caffeine. Zlatkov, A.; Peikov, P.; Gagauzov, I. (Nauchen Inst. Farmakol. Farm., MA, Sofia, Bulg.). Farmatsiya (Sofia, Bulgaria), 41(1), 1-4 (Bulgarian) 1991. CODEN: FMTYA2. ISSN: 0428-0296.

AB Aminolysis of 8-[(2-bromoethyl)amino]caffeine with 4 equiv RNHR1 [R = H, R1 = CH<sub>2</sub>CHMeOH, CHEtCH<sub>2</sub>OH, CH<sub>2</sub>CH<sub>2</sub>Ph, CHMeCH<sub>2</sub>Ph; R = Me, PhCH<sub>2</sub>, R1 = CH<sub>2</sub>CH<sub>2</sub>OH; RR1N = (CH<sub>2</sub>)<sub>6</sub>N, 3-(4-bromophenyl)morpholino] at 100.degree. for 3-180 min gave 55-75% title compds., identified by their IR and UV spectra.

L29 ANSWER 145 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 136611-64-8 REGISTRY

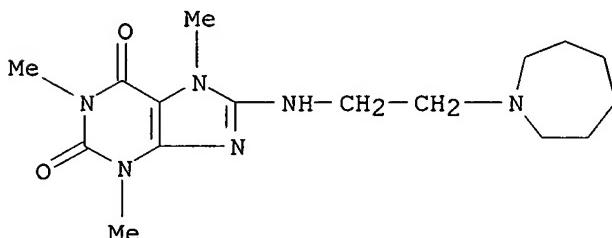
CN 1H-Purine-2,6-dione, 8-[(2-(hexahydro-1H-azepin-1-yl)ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C16 H26 N6 O2

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1962 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 124:278873 Synthesis, toxicological and pharmacological investigations of 8-basic substituted derivatives of caffeine. Danchev, N.; Zlatkov, A.; Peikov, P. (Dep. Pharmacol., Faculty Pharmacy, Sofia, Bulg.). Dokladi na Bulgarskata Akademiya na Naukite, 48(5), 119-22 (English) 1995. CODEN: DBANEH. ISSN: 0861-1459. Publisher: Izdatelstvo na Bulgarskata Akademiya na Naukite.

AB The prepn. of some new 8-basic substituted derivs. of caffeine and their psychostimulant, hypotensive, antiarrhythmic activity and toxicity is reported.

REFERENCE 2: 115:182936 Synthesis of (2-aminoethyl)amino derivatives of caffeine. Zlatkov, A.; Peikov, P.; Gagauzov, I. (Nauchen Inst. Farmakol.

Farm., MA, Sofia, Bulg.). Farmatsiya (Sofia, Bulgaria), 41(1), 1-4 (Bulgarian) 1991. CODEN: FMTYA2. ISSN: 0428-0296.

AB Aminolysis of 8-[(2-bromoethyl)amino]caffeine with 4 equiv RNHR1 [R = H, R1 = CH<sub>2</sub>CHMeOH, CHEtCH<sub>2</sub>OH, CH<sub>2</sub>CH<sub>2</sub>Ph, CHMeCH<sub>2</sub>Ph; R = Me, PhCH<sub>2</sub>, R1 = CH<sub>2</sub>CH<sub>2</sub>OH; RR1N = (CH<sub>2</sub>)<sub>6</sub>N, 3-(4-bromophenyl)morpholino] at 100.degree. for 3-180 min gave 55-75% title compds., identified by their IR and UV spectra.

L29 ANSWER 146 OF 177 REGISTRY COPYRIGHT 2002 ACS

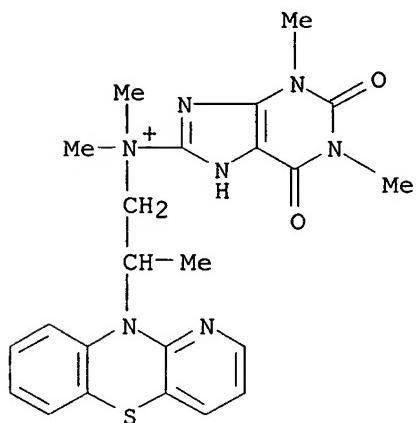
RN 114740-65-7 REGISTRY

CN Dimethyl[2-(10H-pyrido[3,2-b][1,4]benzothiazin-10-yl)propyl](1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)ammonium chloride (6CI) (CA INDEX NAME)

MF C23 H26 N7 O2 S . Cl

SR CAOLD

LC STN Files: CAOLD



● Cl<sup>-</sup>

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L29 ANSWER 147 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 114607-10-2 REGISTRY

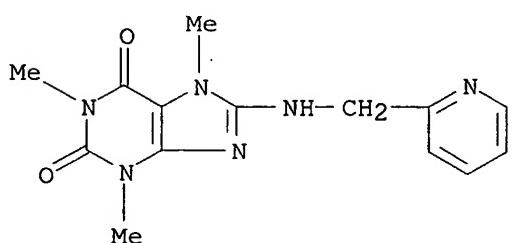
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C14 H16 N6 O2

SR CA

LC STN Files: CA, CAPLUS, CHEMCATS

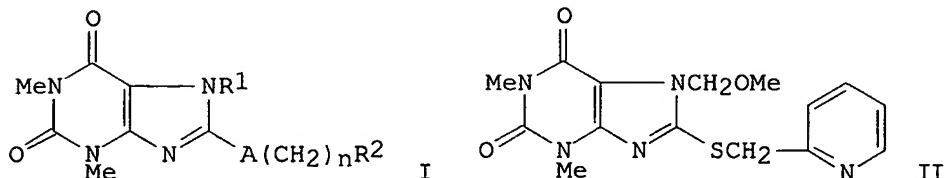


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

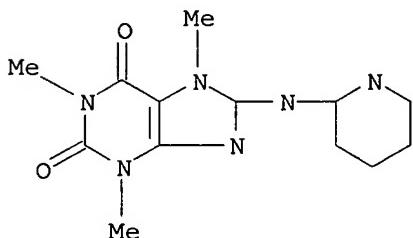
REFERENCE 1: 108:221500 Preparation of theophylline derivatives as gastric antiulcer agents. Hori, Mikio (Suntory, Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 62175483 A2 19870801 Showa, 9 pp. (Japanese). CODEN: JKXXAF.  
APPLICATION: JP 1986-15403 19860127.

GI



AB The title compds. I (R<sub>1</sub> = H, lower alkyl, alkoxyethyl; n = 1-3; when A is S or SO, R<sub>2</sub> is 3-alkyl-2-cyanoguanidyl, pyridyl; when A is O or amino, R<sub>2</sub> is pyridyl), useful as gastric antiulcer agents, were prep'd. Thioetherification of 7-methoxymethyl-8-mercaptoptheophylline with 2-(chloromethyl)pyridine in DMF contg. NaH gave (pyridylmethylthio)theophylline deriv. II. At 100 mg/kg orally, II completely inhibited EtOH/HCl-induced gastric lesion in rats.

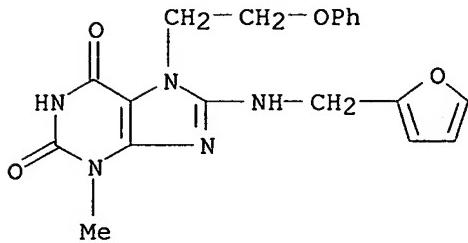
L29 ANSWER 148 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 109443-93-8 REGISTRY  
CN Caffeine, 8-(2-pyridylamino)- (6CI) (CA INDEX NAME)  
MF C13 H14 N6 O2  
SR CAOLD  
LC STN Files: BEILSTEIN\*, CAOLD  
(\*File contains numerically searchable property data)



\*\*\* FRAGMENT DIAGRAM IS INCOMPLETE \*\*\*  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L29 ANSWER 149 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 105522-60-9 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)amino]-3,7-dihydro-3-methyl-7-(2-phenoxyethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H19 N5 O4  
SR CA

LC STN Files: CA, CAPLUS, CASREACT, RTECS\*  
(\*File contains numerically searchable property data)

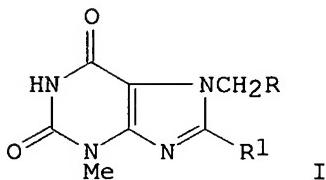


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 105:226150 Synthesis, neurotropic and diuretic activity of 7,8-disubstituted 3-methylxanthines. Samura, B. A.; Fedulova, I. V.; Romanenko, B. A.; Priimenko, B. A.; Chervinskii, A. Yu.; Garmash, S. N.; Troshin, D. A. (Zaporozh. Med. Inst., Zaporozh, USSR). Khimiko-Farmatsevticheskii Zhurnal, 20(1), 52-5 (Russian) 1986. CODEN: KHFZAN. ISSN: 0023-1134.

GI



AB The title compds. I ( $R = Ph$ ,  $CH_2OPh$ ,  $CH(OH)C_6H_4NO_2-p$ ,  $R1 = 2\text{-furylmethylamino}$ , morpholino, hexamethylenimino,  $NHCH_2CH_2OH$ ,  $NET_2$ , piperazino,  $SCH_2CO_2H$ ), useful as psychotropics and diuretics, were prep'd. in 24-94% yields from I ( $R1 = Br$ ) by amination with appropriate amines or by reaction with  $HSCH_2CO_2H$ . The hydrochloride of I [ $R = CH(OH)C_6H_4NO_2-p$ ,  $R1 = piperazino$ ] increased urinary flow 180.7% compared to a control and potentiated narcotic sleep 147.0% compared to a control.

L29 ANSWER 150 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 105522-54-1 REGISTRY

CN 1H-Purine-2,6-dione, 8-[2-furylmethyl]amino]-3,7-dihydro-3-methyl-7-(phenylmethyl)- (9CI) (CA INDEX NAME)

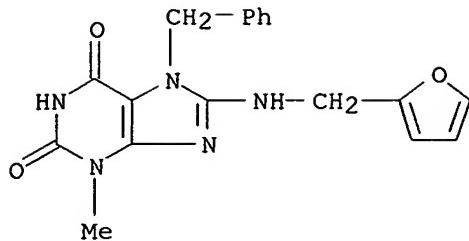
FS 3D CONCORD

MF C18 H17 N5 O3

SR CA

LC STN Files: CA, CAPLUS, CASREACT, RTECS\*

(\*File contains numerically searchable property data)

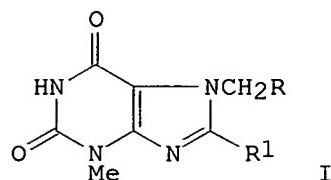


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

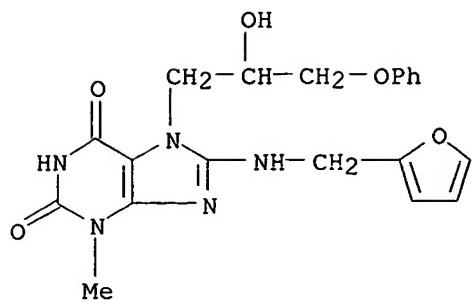
REFERENCE 1: 105:226150 Synthesis, neurotropic and diuretic activity of 7,8-disubstituted 3-methylxanthines. Samura, B. A.; Fedulova, I. V.; Romanenko, B. A.; Priimenko, B. A.; Chervinskii, A. Yu.; Garmash, S. N.; Troshin, D. A. (Zaporozh. Med. Inst., Zaporozh, USSR). Khimiko-Farmatsevticheskii Zhurnal, 20(1), 52-5 (Russian) 1986. CODEN: KHFZAN. ISSN: 0023-1134.

GI



AB The title compds. I ( $R = Ph$ ,  $CH_2OPh$ ,  $CH(OH)C_6H_4NO_2-p$ ,  $R1 = 2$ -furylmethylamino, morpholino, hexamethylenimino,  $NHCH_2CH_2OH$ ,  $NET_2$ , piperazino,  $SCH_2CO_2H$ ), useful as psychotropics and diuretics, were prep'd. in 24-94% yields from I ( $R1 = Br$ ) by amination with appropriate amines or by reaction with  $HSCH_2CO_2H$ . The hydrochloride of I [ $R = CH(OH)C_6H_4NO_2-p$ ,  $R1 = piperazino$ ] increased urinary flow 180.7% compared to a control and potentiated narcotic sleep 147.0% compared to a control.

L29 ANSWER 151 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 102838-10-8 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[ (2-furylmethyl)amino]-3,7-dihydro-7-(2-hydroxy-3-phenoxypropyl)-3-methyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H21 N5 O5  
SR CA  
LC STN Files: CA, CAPLUS, CHEMCATS

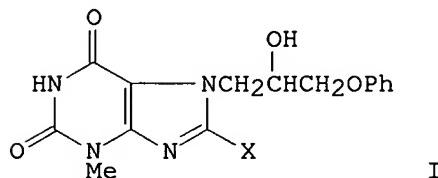


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 105:24103 Synthesis and biological activity of 3-methyl-7-(.beta.-hydroxy-.gamma.-phenoxypropyl)xanthine derivatives. Priimenko, B. A.; Samura, B. A.; Romanenko, N. I.; Fedulova, I. V.; Gnatov, N. I. (Med. Inst., Zaporozhe, USSR). Farmatsevtichni Zhurnal (Kiev) (5), 40-3 (Ukrainian) 1985. CODEN: FRZKAP. ISSN: 0367-3057.

GI



I

AB Refluxing 8-chloro-3-methylxanthine with Ph glycidyl ether in PrOH contg. Et<sub>3</sub>N gave 77.6% title compd. I (X = Cl), which reacted with RH (R = piperidino, morpholino, hexamethylenimino, Et<sub>2</sub>N, PhCH<sub>2</sub>NH, HOCH<sub>2</sub>CH<sub>2</sub>NH, cyclohexylamino, 2-furfuryl amino, homoveratryl amino) in refluxing aq. DMF to give 9 corresponding I (X = R) in 76.5-98.0% yield.

L29 ANSWER 152 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 102212-47-5 REGISTRY

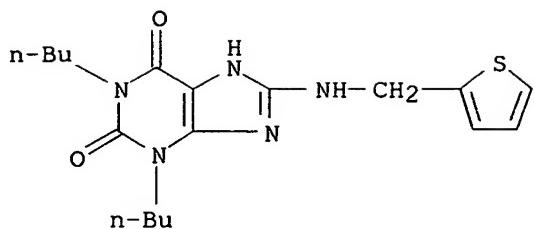
CN 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-[(2-thienylmethyl)amino]-(9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C18 H25 N5 O2 S

SR CA

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, TOXCENTER  
(\*File contains numerically searchable property data)

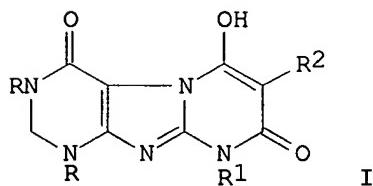


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 105:6481 Antiinflammatory activity of substituted 6-hydroxypyrimido[2,1-f]purine-2,4,8(1H,3H,9H)-triones. Atypical nonsteroidal antiinflammatory agents. Blythin, David J.; Kaminski, James J.; Domalski, Martin S.; Spitzer, James; Solomon, Daniel M.; Conn, David J.; Wong, Shing Chun; Verbiar, Laura Lehman; Bober, Loretta A.; et al. (Pharm. Res. Div., Schering-Plough Corp., Bloomfield, NJ, 07003, USA). Journal of Medicinal Chemistry, 29(6), 1099-113 (English) 1986. CODEN: JMCMAR. ISSN: 0022-2623.

GI



AB Antiinflammatory pyrimido[2,1-f]purine triones I (R = Me, Bu; R<sub>1</sub> = Ph, PhCH<sub>2</sub>, FC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, 4-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, 2-thienylmethyl, PhCHMe, cyclohexymethyl; R<sub>2</sub> = H, Me, Pr, Me<sub>2</sub>CH, Bu, PhCH<sub>2</sub>, EtOCH<sub>2</sub>CH<sub>2</sub>, EtSCH<sub>2</sub>CH<sub>2</sub>, etc.) were prep'd. and their structures were detd. via x-ray crystallog. Semiempirical MO calcns. showed the relative stability of the possible isomers and tautomers of I. A biol. profile of the class, and of several of the more potent analogs, in several antiinflammatory models, including the adjuvant-induced arthritis and the collagen II models, were defined. Several I possess extremely low ulcerogenic effects in spite of exhibiting cyclooxygenase inhibition. A preliminary bioavailability study of I (R, R<sub>1</sub>, R<sub>2</sub> = Me, 4-FC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, Ph; Me, PhCH<sub>2</sub>, Me<sub>2</sub>C:CHCH<sub>2</sub>) was presented. I constitute a class of drugs that shows interesting potential antiarthritic activity and also exhibits an activity profile different from that of the std. drugs. Toxicol. properties have precluded the further development of compds. within this group, although related structural types are being investigated.

L29 ANSWER 153 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 102212-38-4 REGISTRY

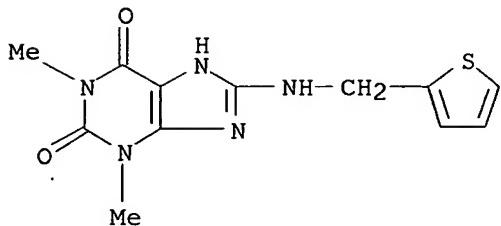
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(2-thienylmethyl)amino]-(9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C12 H13 N5 O2 S

SR CA

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, TOXCENTER  
(\*File contains numerically searchable property data)

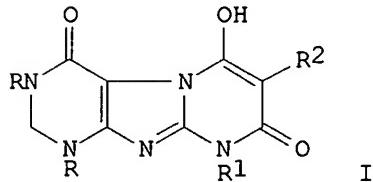


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

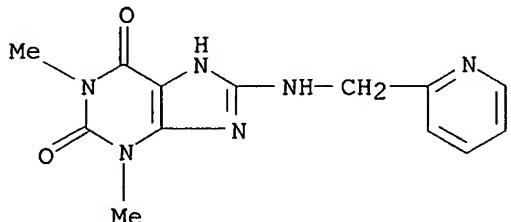
REFERENCE 1: 105:6481 Antiinflammatory activity of substituted 6-hydroxypyrimido[2,1-f]purine-2,4,8(1H,3H,9H)-triones. Atypical nonsteroidal antiinflammatory agents. Blythin, David J.; Kaminski, James J.; Domalski, Martin S.; Spitzer, James; Solomon, Daniel M.; Conn, David J.; Wong, Shing Chun; Verbiar, Laura Lehman; Bober, Loretta A.; et al. (Pharm. Res. Div., Schering-Plough Corp., Bloomfield, NJ, 07003, USA). Journal of Medicinal Chemistry, 29(6), 1099-113 (English) 1986. CODEN: JMCMAR. ISSN: 0022-2623.

GI



AB Antiinflammatory pyrimido[2,1-f]purine triones I (R = Me, Bu; R1 = Ph, PhCH<sub>2</sub>, FC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, 4-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, 2-thienylmethyl, PhCHMe, cyclohexymethyl; R2 = H, Me, Pr, Me<sub>2</sub>CH, Bu, PhCH<sub>2</sub>, EtOCH<sub>2</sub>CH<sub>2</sub>, EtSCH<sub>2</sub>CH<sub>2</sub>, etc.) were prep'd. and their structures were detd. via x-ray crystallog. Semiempirical MO calcns. showed the relative stability of the possible isomers and tautomers of I. A biol. profile of the class, and of several of the more potent analogs, in several antiinflammatory models, including the adjuvant-induced arthritis and the collagen II models, were defined. Several I possess extremely low ulcerogenic effects in spite of exhibiting cyclooxygenase inhibition. A preliminary bioavailability study of I (R, R1, R2 = Me, 4-FC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, Ph; Me, PhCH<sub>2</sub>, Me<sub>2</sub>C:CHCH<sub>2</sub>) was presented. I constitute a class of drugs that shows interesting potential antiarthritic activity and also exhibits an activity profile different from that of the std. drugs. Toxicol. properties have precluded the further development of compds. within this group, although related structural types are being investigated.

L29 ANSWER 154 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 102212-37-3 REGISTRY  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(2-pyridinylmethyl)amino]-  
     (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C13 H14 N6 O2  
 SR CA  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, TOXCENTER  
     (\*File contains numerically searchable property data)

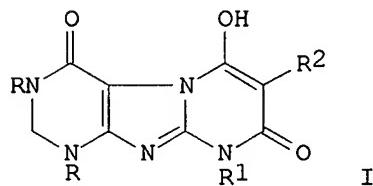


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 105:6481 Antiinflammatory activity of substituted  
 6-hydroxypyrimido[2,1-f]purine-2,4,8(1H,3H,9H)-triones. Atypical  
 nonsteroidal antiinflammatory agents. Blythin, David J.; Kaminski, James  
 J.; Domalski, Martin S.; Spitzer, James; Solomon, Daniel M.; Conn, David  
 J.; Wong, Shing Chun; Verbiar, Laura Lehman; Bober, Loretta A.; et al.  
 (Pharm. Res. Div., Schering-Plough Corp., Bloomfield, NJ, 07003, USA).  
 Journal of Medicinal Chemistry, 29(6), 1099-113 (English) 1986. CODEN:  
 JMCMAR. ISSN: 0022-2623.

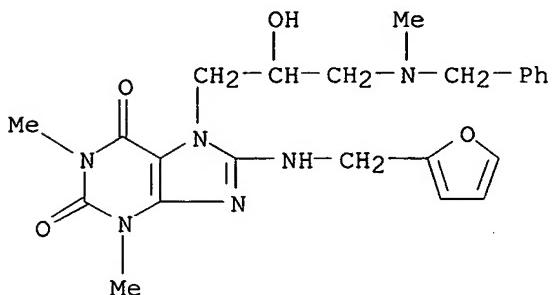
GI



AB Antiinflammatory pyrimido[2,1-f]purine triones I (R = Me, Bu; R1 = Ph,  
 PhCH2, FC6H4CH2, ClC6H4CH2, 4-MeOC6H4CH2, 2-thienylmethyl, PhCHMe,  
 cyclohexymethyl; R2 = H, Me, Pr, Me2CH, Bu, PhCH2, EtOCH2CH2, EtSCH2CH2,  
 etc.) were prep'd. and their structures were detd. via x-ray crystallog.  
 Semiempirical MO calcns. showed the relative stability of the possible  
 isomers and tautomers of I. A biol. profile of the class, and of several  
 of the more potent analogs, in several antiinflammatory models, including  
 the adjuvant-induced arthritis and the collagen II models, were defined.  
 Several I possess extremely low ulcerogenic effects in spite of exhibiting  
 cyclooxygenase inhibition. A preliminary bioavailability study of I (R,  
 R1, R2 = Me, 4-FC6H4CH2, Ph; Me, PhCH2, Me2C:CHCH2) was presented. I  
 constitute a class of drugs that shows interesting potential antiarthritic

activity and also exhibits an activity profile different from that of the std. drugs. Toxicol. properties have precluded the further development of compds. within this group, although related structural types are being investigated.

L29 ANSWER 155 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 98624-74-9 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[ (2-furanyl methyl) amino]-3,7-dihydro-7-[2-hydroxy-3-[methyl(phenylmethyl) amino]propyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C23 H28 N6 O4  
SR CA  
LC STN Files: CA, CAPLUS

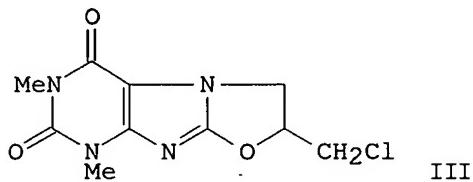
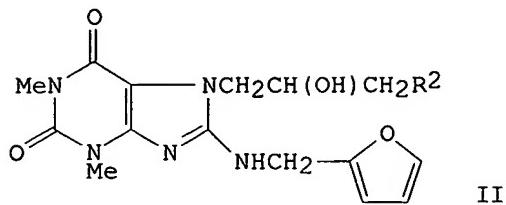
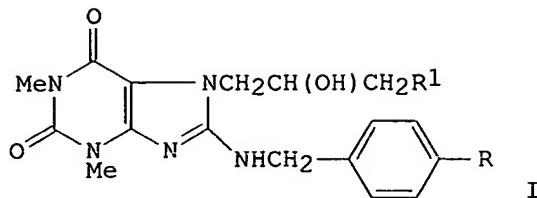


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 103:160471 Synthesis of new 7,8-alkylamino derivatives of theophylline. Pawłowski, Maciej; Gorczyca, Maria; Lucka-Sobstel, Barbara (Dep. Pharm. Chem., Sch. Med., Krakow, 31-065, Pol.). Acta Poloniae Pharmaceutica, 42(1), 4-10 (Polish) 1985. CODEN: APPHAX. ISSN: 0001-6837.

GI



AB In a study on the effect of alkylamino substituents on the biol. activity of theophylline-derived compds., five I ( $R = H$ ,  $R1 = 2$ - and 4-chloro- and 2,4-dichlorobenzylamino, isolated as the HCl salts;  $R = H$ ,  $R1 = 2$ -furfurylamino; isolated as the maleate;  $R = OMe$ ,  $R1 = 2$ -furfurylamino) and two II [ $R2 = N(CH_2Ph)_2$  and  $NMeCH_2Ph$ ] were prep'd. in 52-90% yields by heating in EtOH/KOH the appropriately  $R$ -substituted I ( $R1 = Cl$ ) and II ( $R2 = Cl$ ), resp., with the corresponding amines. The starting I ( $R1 = Cl$ ) and II ( $R2 = Cl$ ) were obtained by aminolysis of III with  $PhCH_2NH_2$ ,  $4-MeOC_6H_4CH_2NH_2$ , and 2-furfurylamine, resp. I ( $R = MeO$ ,  $R1 = Cl$ ) and II [ $R2 = Cl$ ,  $N(CH_2Ph)_2$ ] were converted into the O-acetoxy derivs. by treating with  $Ac_2O$ .

L29 ANSWER 156 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 98624-72-7 REGISTRY

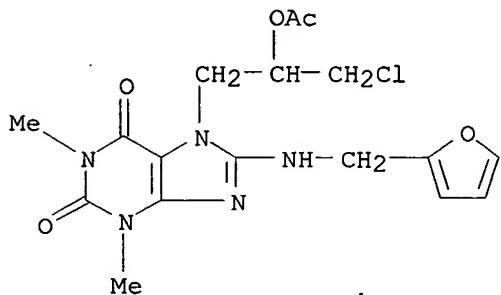
CN 1H-Purine-2,6-dione, 7-[2-(acetyloxy)-3-chloropropyl]-8-[(2-furylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C17 H20 Cl N5 O5

SR CA

LC STN Files: CA, CAPLUS

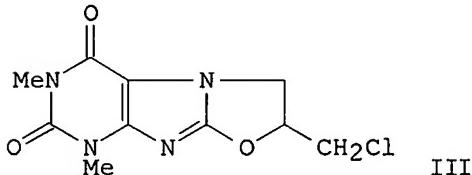
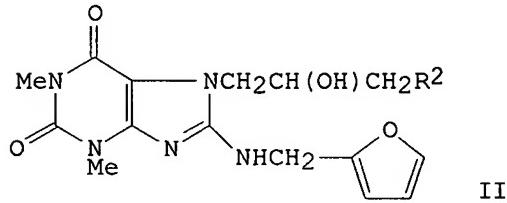
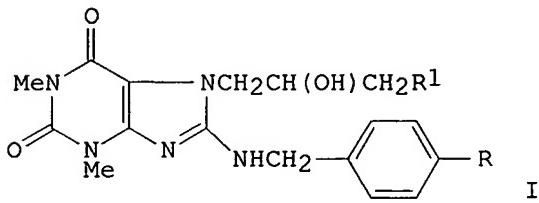


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 103:160471 Synthesis of new 7,8-alkylamino derivatives of theophylline. Pawłowski, Maciej; Gorczyca, Maria; Lucka-Sobstel, Barbara (Dep. Pharm. Chem., Sch. Med., Krakow, 31-065, Pol.). Acta Poloniae Pharmaceutica, 42(1), 4-10 (Polish) 1985. CODEN: APPHAX. ISSN: 0001-6837.

GI



AB In a study on the effect of alkylamino substituents on the biol. activity of theophylline-derived compds., five I (R = H, R1 = 2- and 4-chloro- and 2,4-dichlorobenzylamino, isolated as the HCl salts; R = H, R1 = 2-furfurylamino; isolated as the maleate; R = OMe, R1 = 2-furfurylamino) and two II [R2 = N(CH2Ph)2 and NMeCH2Ph] were prep'd. in 52-90% yields by heating in EtOH/KOH the appropriately R-substituted I (R1 = Cl) and II (R2 = Cl), resp., with the corresponding amines. The starting I (R1 = Cl) and II (R2 = Cl) were obtained by aminolysis of III with PhCH2NH2, 4-MeOC6H4CH2NH2, and 2-furfurylamine, resp. I (R = MeO, R1 = Cl) and II [R2 = Cl, N(CH2Ph)2] were converted into the O-acetoxy derivs. by treating with Ac2O.

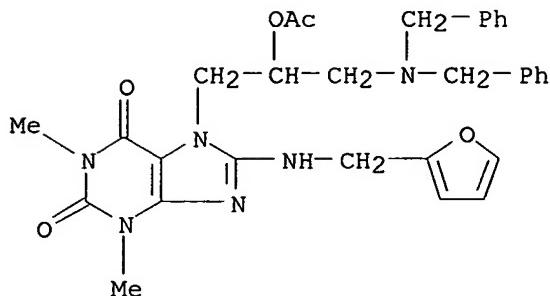
L29 ANSWER 157 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 98624-71-6 REGISTRY

CN 1H-Purine-2,6-dione, 7-[2-(acetyloxy)-3-[bis(phenylmethyl)amino]propyl]-8-[(2-furylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C31 H34 N6 O5  
SR CA  
LC STN Files: CA, CAPLUS

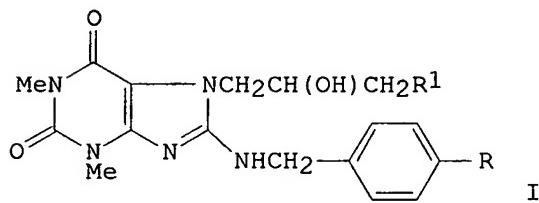


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

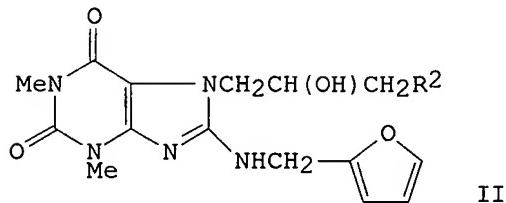
1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 103:160471 Synthesis of new 7,8-alkylamino derivatives of theophylline. Pawłowski, Maciej; Gorczyca, Maria; Lucka-Sobstel, Barbara (Dep. Pharm. Chem., Sch. Med., Krakow, 31-065, Pol.). Acta Poloniae Pharmaceutica, 42(1), 4-10 (Polish) 1985. CODEN: APPHAX. ISSN: 0001-6837.

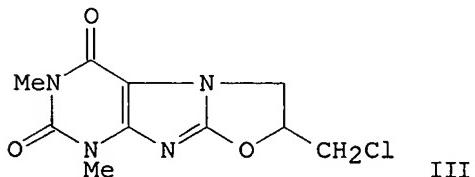
GI



I



II



III

AB In a study on the effect of alkylamino substituents on the biol. activity

Searched by: Mary Hale 308-4258 CM-1 1E01

of theophylline-derived compds., five I (R = H, R1 = 2- and 4-chloro- and 2,4-dichlorobenzylamino, isolated as the HCl salts; R = H, R1 = 2-furfurylamino; isolated as the maleate; R = OMe, R1 = 2-furfurylamino) and two II [R2 = N(CH<sub>2</sub>Ph)<sub>2</sub> and NMeCH<sub>2</sub>Ph] were prep'd. in 52-90% yields by heating in EtOH/KOH the appropriately R-substituted I (R1 = Cl) and II (R2 = Cl), resp., with the corresponding amines. The starting I (R1 = Cl) and II (R2 = Cl) were obtained by aminolysis of III with PhCH<sub>2</sub>NH<sub>2</sub>, 4-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>NH<sub>2</sub>, and 2-furfurylamine, resp. I (R = MeO, R1 = Cl) and II [R2 = Cl, N(CH<sub>2</sub>Ph)<sub>2</sub>] were converted into the O-acetoxy derivs. by treating with Ac<sub>2</sub>O.

L29 ANSWER 158 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 98624-70-5 REGISTRY

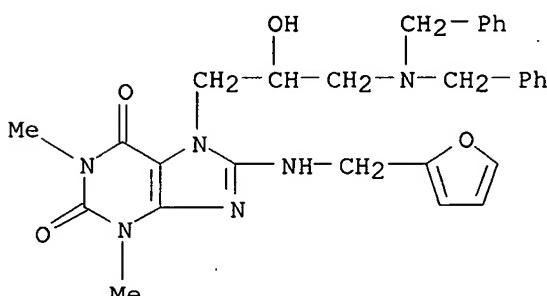
CN 1H-Purine-2,6-dione, 7-[3-[bis(phenylmethyl)amino]-2-hydroxypropyl]-8-[(2-furanylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C29 H32 N6 O4

SR CA

LC STN Files: CA, CAPLUS, CHEMCATS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1962 TO DATE)

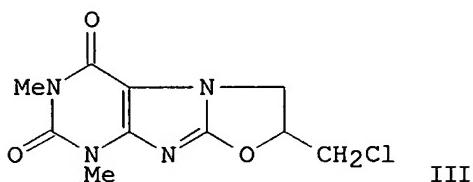
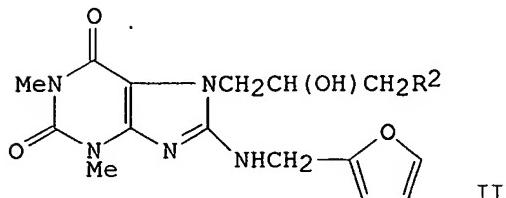
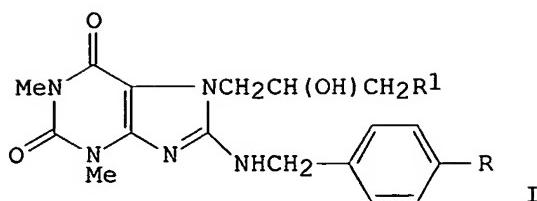
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 124:102475 7-[3-(Dibenzylamino)-2-hydroxypropyl]-8-(furfurylamino)theophylline. Karczmarzyk, Zbigniew; Karolak-Wojciechowska, Janina; Pawłowski, Maciej (Dep. Chem., Agric. Teach. Univ., Siedlce, 08-110, Pol.). Acta Crystallographica, Section C: Crystal Structure Communications, C51(12), 2608-10 (English) 1995. CODEN: ACSCEE. ISSN: 0108-2701. Publisher: Munksgaard.

AB The theophylline moiety of the title compd., 7-[3-(dibenzylamino)-2-hydroxypropyl]-8-(furfurylamino)-3,7-dihydro-1,3-dimethyl-1H-purine-2,6-dione, C<sub>29</sub>H<sub>32</sub>N<sub>6</sub>O<sub>4</sub>, is planar. The conformation of the 7-aminohydroxyalkyl substituent may be influenced by an O-H..cntdot..cntdot..cntdot.N intramol. H bond and the structure is stabilized by an N-H..cntdot..cntdot..cntdot.O intermol. bond. Crystallog. data and at. coordinates are given.

REFERENCE 2: 103:160471 Synthesis of new 7,8-alkylamino derivatives of theophylline. Pawłowski, Maciej; Gorczyca, Maria; Lucka-Sobstel, Barbara (Dep. Pharm. Chem., Sch. Med., Krakow, 31-065, Pol.). Acta Poloniae Pharmaceutica, 42(1), 4-10 (Polish) 1985. CODEN: APPHAX. ISSN: 0001-6837.

GI



AB In a study on the effect of alkylamino substituents on the biol. activity of theophylline-derived compds., five I ( $R = H$ ,  $R1 = 2$ - and 4-chloro- and 2,4-dichlorobenzylamino, isolated as the HCl salts;  $R = H$ ,  $R1 = 2$ -furfurylamino; isolated as the maleate;  $R = OMe$ ,  $R1 = 2$ -furfurylamino) and two II [ $R2 = N(CH_2Ph)_2$  and  $NMeCH_2Ph$ ] were prep'd. in 52-90% yields by heating in EtOH/KOH the appropriately  $R$ -substituted I ( $R1 = Cl$ ) and II ( $R2 = Cl$ ), resp., with the corresponding amines. The starting I ( $R1 = Cl$ ) and II ( $R2 = Cl$ ) were obtained by aminolysis of III with  $PhCH_2NH_2$ ,  $4$ -MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>NH<sub>2</sub>, and 2-furfurylamine, resp. I ( $R = MeO$ ,  $R1 = Cl$ ) and II [ $R2 = Cl$ ,  $N(CH_2Ph)_2$ ] were converted into the O-acetoxy derivs. by treating with Ac<sub>2</sub>O.

L29 ANSWER 159 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 98624-69-2 REGISTRY

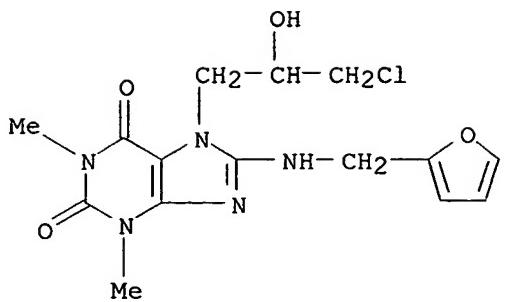
CN 1H-Purine-2,6-dione, 7-(3-chloro-2-hydroxypropyl)-8-[(2-furylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C15 H18 Cl N5 O4

SR CA

LC STN Files: CA, CAPLUS

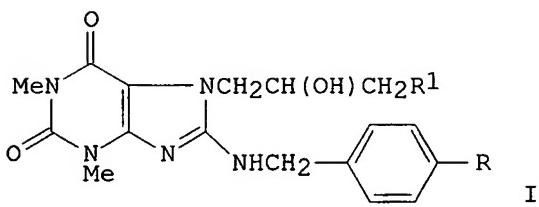


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

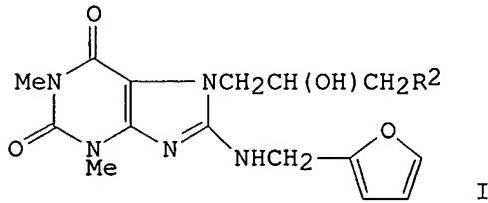
1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 103:160471 Synthesis of new 7,8-alkylamino derivatives of theophylline. Pawłowski, Maciej; Gorczyca, Maria; Lucka-Sobstel, Barbara (Dep. Pharm. Chem., Sch. Med., Krakow, 31-065, Pol.). Acta Poloniae Pharmaceutica, 42(1), 4-10 (Polish) 1985. CODEN: APPHAX. ISSN: 0001-6837.

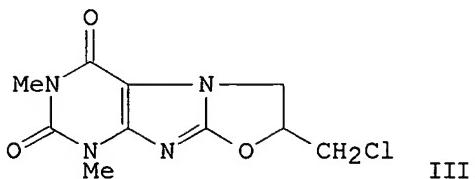
GI



I



II



III

AB In a study on the effect of alkylamino substituents on the biol. activity of theophylline-derived compds., five I (R = H, R1 = 2- and 4-chloro- and 2,4-dichlorobenzylamino, isolated as the HCl salts; R = H, R1 = 2-furfurylamino; isolated as the maleate; R = OMe, R1 = 2-furfurylamino) and two II [R2 = N(CH2Ph)2 and NMeCH2Ph] were prep'd. in 52-90% yields by

heating in EtOH/KOH the appropriately R-substituted I (R1 = Cl) and II (R2 = Cl), resp., with the corresponding amines. The starting I (R1 = Cl) and II (R2 = Cl) were obtained by aminolysis of III with PhCH2NH2, 4-MeOC6H4CH2NH2, and 2-furfurylamine, resp. I (R = MeO, R1 = Cl) and II [R2 = Cl, N(CH2Ph)2] were converted into the O-acetoxy derivs. by treating with Ac2O.

L29 ANSWER 160 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 97790-68-6 REGISTRY

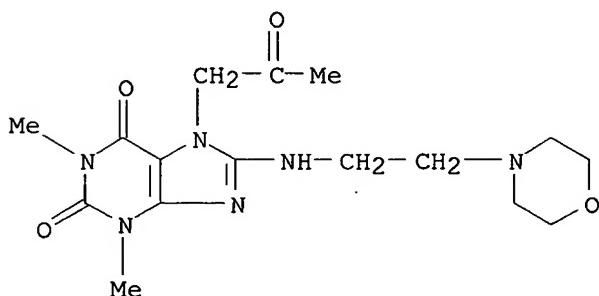
CN Theophylline, 7-acetonyl-8-[ (2-morpholinoethyl)amino]-, hydrochloride (7CI) (CA INDEX NAME)

MF C16 H24 N6 O4 . x Cl H

SR CAOLD

LC STN Files: CA, CAOLD, CAPLUS

CRN (979-53-3)



● x HCl

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 62:51641 Synthesis in the theophylline series. XI. Synthesis of 7-acetonyltheophyllines. J. Prakt. Chem., 26(3-4), 155-8 (Unavailable) 1964.

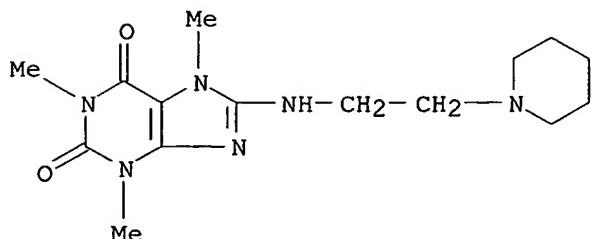
AB I or the Br analog with dialkylaminoalkylamines yielded the corresponding II under mild conditions. I (27 g.) and 11.6 g. Et2NCH2CH2NH2 in 100 cc. iso-PrOH refluxed 5 hrs. yielded 25 g. II (R = H, R1 = CH2CH2NET2) (V), m. 143-5.degree. (repptd. from MePh with petr. ether); V. HCl m. 288-90.degree.; V. MeBr m. 297-9.degree.. Similarly were prep'd. the following II (R, R1, and m.ps. of base and HCl salt given): H, Et2N(CH2)3, 118-20.degree., 260-2.degree. (methobromide m. 238-40.degree.); H, Me2N(CH2)3, 125-7.degree., 240-2.degree. (methobromide m. 225-7.degree.); Me, Et2NCH2CH2, 98, -- (hygroscopic); Me, Me2NCH2CH2, 114-16.degree., 254-6.degree.; H, 2-piperidinoethyl, 158-60.degree., --; H, 2-morpholinoethyl, 198-200.degree., 266-8.degree.; H, 3-cyclohexylaminopropyl, 120-2.degree., 325-7.degree.. Similarly was prep'd. II [(R1 = ) 4-methylpiperazino)], m. 135-7.degree.; HCl salt m. 272-4.degree.. II did not reach the pharmacol. activity of theophylline, caffeine, or 7-acetonyltheophylline.

L29 ANSWER 161 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 97407-28-8 REGISTRY

CN Caffeine, 8-[ (2-piperidinoethyl)amino]-, hydrochloride (7CI) (CA INDEX

NAME)  
MF C15 H24 N6 O2 . x Cl H  
SR CAOLD  
LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS  
(\*File contains numerically searchable property data)  
CRN (33236-60-1)



●x HCl

2 REFERENCES IN FILE CA (1962 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 59:75376 8-Caffeinylalkylenediamines. Klosa, Josef (Delmar Chemicals Ltd.). US 3094529 19630618, 3 pp. (Unavailable). APPLICATION: US 19590911.

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) have a strong and sustained hypotensive action. Thus, 0.1 mole .beta.-(8-caffeinyl)aminoethyl chloride and 0.2 mole piperidine were refluxed with 40 ml. alc. 8 hrs. and cooled, the solid filtered off and dissolved in H<sub>2</sub>O, and the soln. made strongly alk. to give 1-piperidino-2-(8-caffeinyl)aminoethylene, m. 198-200.degree. (alc.); hydrochloride, m. 178-80.degree., 225-7.degree., and 268.degree. (decompn.). Similarly, prep'd. were I (R, n, R', and m.p. given): H, morpholino, 2, 181-3.degree. (alc.) (hydrochloride m. 220-2.degree.; dihydrochloride m. 170.degree. and 247-9.degree.); H, pyrrolidino, 3, 184-5.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether); H, NHPh, 3, 159-61.degree. (alc.); H, NHCHMeCH<sub>2</sub>Ph, 3, 163-5.degree. (alc.). By another method, 11 g. 8-chlorocaffeine was mixed with 8 ml. N-(hydroxyethyl)propylenediamine at 140-60.degree.; the temp. rose to 180.degree.. The mixt. was heated 0.5 hr., the solidified mass heated 10 min., cooled, and taken up in alc., an equal vol. H<sub>2</sub>O added, the soln. made strongly alk. the milky cloudiness solidified on cooling to give I (R = H, R<sub>1</sub> = NHCH<sub>2</sub>CH<sub>2</sub>OH, n = 3) m. 175-7.degree. (H<sub>2</sub>O). Similarly prep'd. were I (R, R', n, and m.p. given): H, NHCH<sub>2</sub>CH<sub>2</sub>OH, 2, 195-7.degree.; H, N(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>, 2, 142-4.degree..

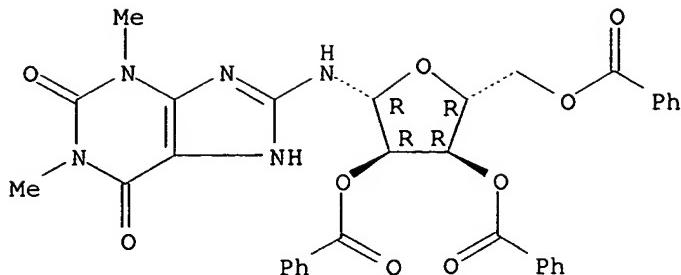
REFERENCE 2: 58:33375 Caffeine-8-alkylene diamines. Klosa, Josef (Privat-Lab., Berlin Zehlendorf, Germany). J. Prakt. Chem., 18, 97-106 (Unavailable) 1962.

AB The title compds. were prep'd. by reaction of 8-chloro- or 8-bromocaffeine (I or II) and alkylene diamines or by treatment of 8-(.beta.-chloroalkyl)alkylamino- or aminocaffeine with primary or secondary bases. 8-(.beta.-Hydroxyethyl)aminocaffeine (10 g.) was added in portions to 10 ml. SOCl<sub>2</sub>, the mixt. heated 20-30 min. on a steam bath, and washed many times with refluxing C<sub>6</sub>H<sub>6</sub> to give 11 g. 8-(.beta.-chloroethyl)aminocaffeine (III), m. 225-7.degree. (MeOH). Similarly, 50

g. 8-(.gamma.-hydroxypropyl)amino-caffeine and 100 ml. SOC12. gave 55 g.  
 8-(.beta.-chloropropyl)aminocaffeine (IV), m. 210-12.degree. (EtOH), and  
 40 g. 8-(.beta.-hydroxyethyl)-methylaminocaffeine and 40 ml. SOC12  
 refluxed 2 hrs. and then n2poured onto ice and neutralized with dil. NH3  
 gave 8-(.beta.-chloroethyl)methylaminocaffeine (V). I (22 g.) and 23 g.  
 Et2NCH2-CH2NH2 were rubbed together, heated to 140.degree. to effect  
 soln., and then refluxed 20 min. at 150-70.degree.. The mixt. was cooled,  
 dissolved in hot EtOH, cooled, and filtered and the crystals dissolved in  
 EtOH, treated with HCl-EtOH, and then with double the vol. of Et2O to give  
 80% N,N-diethyl-N'-(cafein-8-yl)ethylenediamine hydrochloride, m.  
 288-90.degree.; free base m. 186-8.degree. (C6H6-petr. ether);  
 methobromide m. 230.degree.. I (44 g.) and 42 ml. Et2N(CH2)3NH2 heated a  
 few min. at 160-70.degree. gave a mixt. which soon solidified and was  
 purified by washing twice with refluxing EtOH, pptg. 80%  
 N,N-diethyl-N'-(cafein-8-yl)trimethylenediamine hydrochloride, m.  
 222-4.degree. (Et-OH-Et2O); free base m. 158-60.degree. (C6H6-petr. ether  
 or PhMe-petr. ether); methobromide m. 226.degree.; methiodide m.  
 244-6.degree. (MeOH). The following compds. were similarly prep'd.  
 (product, % yield, m.p., crystn. solvent; hydrochloride m.p. given):  
 N,N-dimethyl-N'-(cafein-8-yl)trimethylenediamine, 75-80, 173-5.degree.,  
 C6H6-petr. ether, 268-70.degree.; N-cyclohexyl-N'-(cafein-8-yl)-  
 trimetnylenediamine, --, 136-8.degree., C6H6-petr. ether, 240-2.degree.  
 (dihydrochloride m. 240.degree.); N-methyl-N-(cafein-8-yl)-N',N'-  
 diethylethylenediamine, --, 145-7.degree., --, --, N-ethyl-N-(cafein-8-  
 yl)-N',N'-diethytethylenediamine, --, 138-40.degree., C6H6-petr. ether,  
 --. V (28 g.), 10 ml. pyrrolidine, and 8 g. anhyd. K2CO3 was refluxed 5-6  
 hrs. in 250 ml. 96% EtOH and the soln. filtered hot and reduced to half  
 vol. to give 22 g. 1-(cafein-8-yl)methylamino-2-pyrrolidinoethane, m.  
 70-2.degree. (C6H6-petr. ether). The following compds. were similarly  
 prep'd. from I, III, or IV and the appropriate amines (product, m.p.,  
 crystn. solvent, hydrochloride m.p. given): 1-piperidino-2-(cafein-8-yl)-  
 ethane, 198-200.degree., EtOH, 268.degree. (decompn.);  
 1-morpholino-2-(cafein-8-yl)ethane, 181-3.degree., EtOH, 220-2.degree.  
 [dihydrochloride m. 247-9.degree. (decompn.)]; N-benzyl-N'-(cafein-8-  
 yl)ethylenediamine, --, --, 228-30.degree.; N,N-dibenzyl-N'-(cafein-8-  
 yl)ethylenediamine, --, --, 195-7.degree.; N-isoamyl-N'-(cafein-8-  
 yl)ethylenediamine, --, --, 223-5.degree.; 1-piperidino-3-(cafein-8-  
 yl)aminopropane, 173-5.degree., C6H6-petr. ether, --; 1-pyrrolidino-3-  
 (cafein-8-yl)aminopropane, 165-7.degree., C6H6-Petr. ether, --;  
 N-phenyl-N'-(cafein-8-yl)trimethyl-enediamine, 159-61.degree., EtOH, --;  
 N-(cafein-8-yl)-N'-(1-methylphenethyl)trimethylenediamine, 163-5.degree.,  
 EtOH, --; N-(cafein-8-yl)- N'-(1-hydroxyethyl)trimethylenediamine,  
 175-7.degree., H2O, --; N-(cafein-8-yl)-N',N'-bis(2-  
 hydroxyethyl)ethylenediamine, 142-4.degree., EtOH, --;  
 8-(4-methylpiperazino)caffeine, 148-50.degree., PhMe-petr. ether,  
 344-6.degree. (methobromide m. 315-17.degree.; methiodide m.  
 314-16.degree.); salt between 8-hydroxycaffeine and N,N-  
 diethyltrimethylenediamine, 226.degree., EtOH.

L29 ANSWER 162 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 69435-02-5 REGISTRY  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[ (2,3,5-tri-O-benzoyl-  
    .beta.-D-ribofuranosyl)amino]- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C33 H29 N5 O9  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS  
       (\*File contains numerically searchable property data)

Absolute stereochemistry.

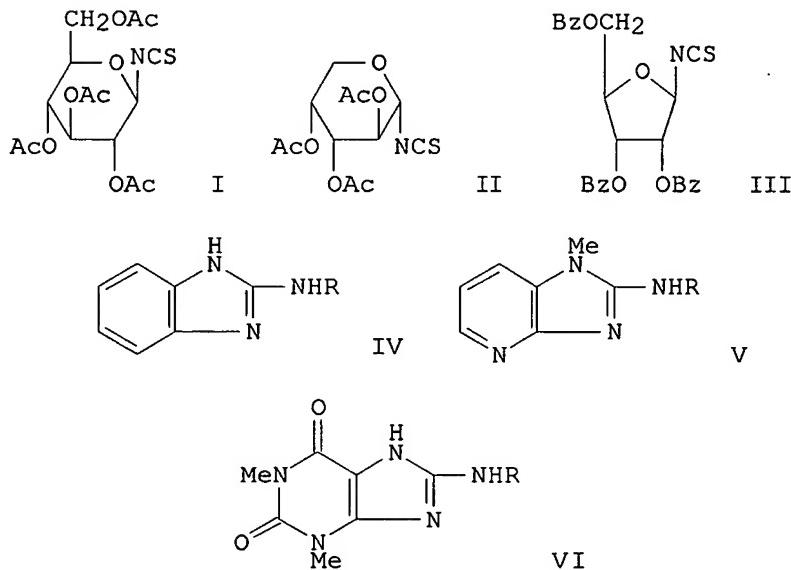


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1962 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

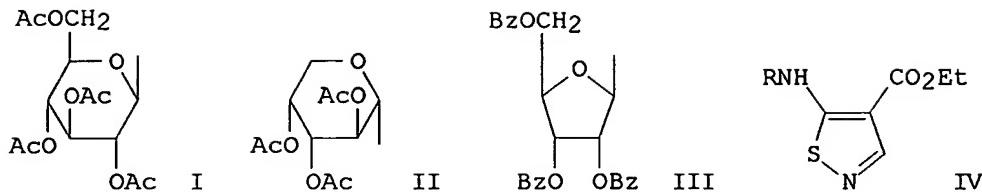
REFERENCE 1: 91:123953 Studies on heterocyclic compounds. Part XXX.  
Cyclodesulfurization reaction of glycosyl thioureides. Takahashi,  
Hiroshi; Nimura, Noriyuki; Obata, Naka; Sakai, Hitomi; Ogura, Haruo (Sch.  
Pharm. Sci., Kitasato Univ., Tokyo, 108, Japan). Chem. Pharm. Bull.,  
27(5), 1153-8 (English) 1979. CODEN: CPBTAL. ISSN: 0009-2363.

GI



AB Reactions of glycosyl isothiocyanates I, II, and III with o-phenylenediamine, 2,3-diaminopyridine or 5,6-diamino-1,3-dimethyluracil gave the corresponding glycosyl thioureides in good yields. Glycosyl thioureides were converted into nucleoside analogs IV, V, or VI (R = glycosyl) in excellent yields through a cyclodesulfurization reaction.

REFERENCE 2: 91:39764 Syntheses of nucleoside analogs using glycosyl isothiocyanate. Ogura, Haruo; Takahashi, Hiroshi (Sch. Pharm. Sci., Kitasato Univ., Tokyo, Japan). Tennen Yuki Kagobutsu Toronkai Koen Yoshishu, 21st, 221-8. Hokkaido Daigaku Nogakubo: Sapporo, Japan. (Japanese) 1978. CODEN: 39NQAF.



AB Various nucleoside analogs contg. isothiazole, isothiazolopyrimidine, fused imidazole, pyrimidothiadiazine, pyrazolopyrimidine, triazole, or triazine moieties were prep'd. by using RNCS (R = I, II, or III). E.g., reaction of RNCS and MeC(NH<sub>2</sub>):CHCO<sub>2</sub>Et gave (glycosylamino)isothiazoles IV and MeC(NH<sub>2</sub>):C(SCNHR)CO<sub>2</sub>Et (V). V readily cyclized to IV.

L29 ANSWER 163 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 69435-01-4 REGISTRY

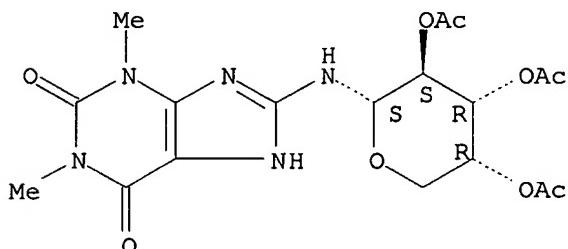
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[ (2,3,4-tri-O-acetyl-.alpha.-D-arabinopyranosyl)amino]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C18 H23 N5 O9

LC STN Files: BEILSTEIN\*, CA, CAPLUS  
(\*File contains numerically searchable property data)

Absolute stereochemistry.

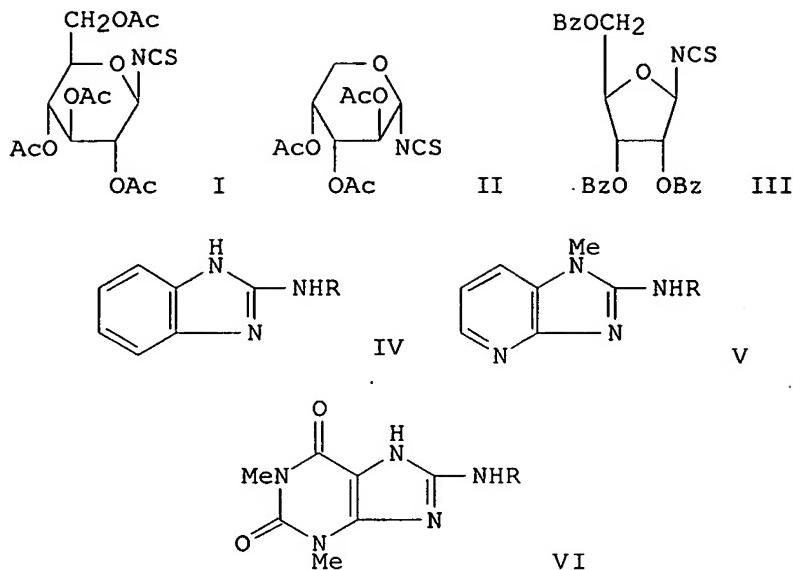


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1962 TO DATE)

2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

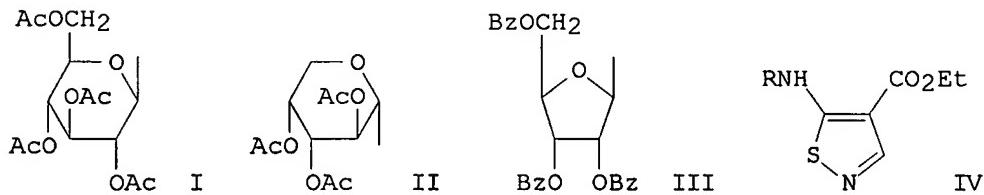
REFERENCE 1: 91:123953 Studies on heterocyclic compounds. Part XXX. Cyclodesulfurization reaction of glycosyl thioureides. Takahashi, Hiroshi; Nimura, Noriyuki; Obata, Naka; Sakai, Hitomi; Ogura, Haruo (Sch. Pharm. Sci., Kitasato Univ., Tokyo, 108, Japan). Chem. Pharm. Bull., 27(5), 1153-8 (English) 1979. CODEN: CPBTAL. ISSN: 0009-2363.



**AB** Reactions of glycosyl isothiocyanates I, II, and III with o-phenylenediamine, 2,3-diaminopyridine or 5,6-diamino-1,3-dimethyluracil gave the corresponding glycosyl thioureides in good yields. Glycosyl thioureides were converted into nucleoside analogs IV, V, or VI ( $R =$  glycosyl) in excellent yields through a cyclodesulfurization reaction.

**REFERENCE 2:** 91:39764 Syntheses of nucleoside analogs using glycosyl isothiocyanate. Ogura, Haruo; Takahashi, Hiroshi (Sch. Pharm. Sci., Kitasato Univ., Tokyo, Japan). Tennen Yuki Kagobutsu Toronkai Koen Yoshishu, 21st, 221-8. Hokkaido Daigaku Nogakubu: Sapporo, Japan. (Japanese) 1978. CODEN: 39NQAF.

GI

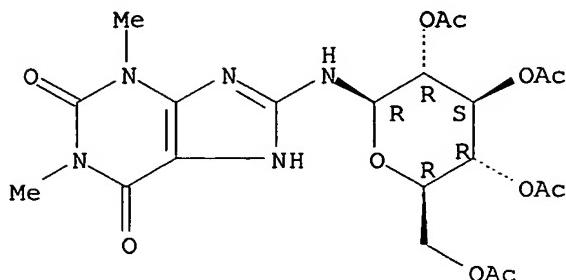


**AB** Various nucleoside analogs contg. isothiazole, isothiazolopyrimidine, fused imidazole, pyrimidothiadiazine, pyrazolopyrimidine, triazole, or triazine moieties were prep'd. by using RNCS ( $R =$  I, II, or III). E.g., reaction of RNCS and  $\text{MeC}(\text{NH}_2):\text{CHCO}_2\text{Et}$  gave (glycosylamino)isothiazoles IV and  $\text{MeC}(\text{NH}_2):\text{C}(\text{SCNHR})\text{CO}_2\text{Et}$  (V). V readily cyclized to IV.

L29 ANSWER 164 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 58911-60-7 REGISTRY  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[ (2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)amino]- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C21 H27 N5 O11

LC STN Files: BEILSTEIN\*, CA, CAPLUS  
(\*File contains numerically searchable property data)

Absolute stereochemistry.

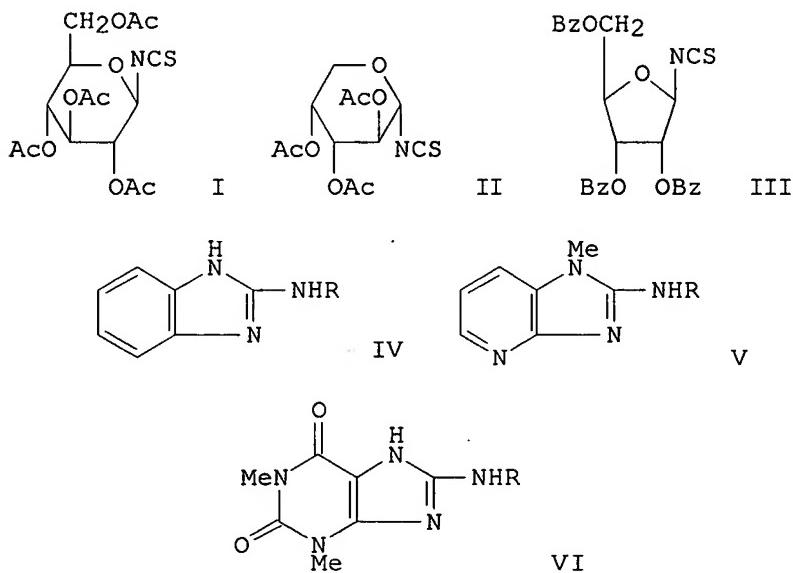


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1962 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 91:123953 Studies on heterocyclic compounds. Part XXX.  
Cyclodesulfurization reaction of glycosyl thioureides. Takahashi,  
Hiroshi; Nimura, Noriyuki; Obata, Naka; Sakai, Hitomi; Ogura, Haruo (Sch.  
Pharm. Sci., Kitasato Univ., Tokyo, 108, Japan). Chem. Pharm. Bull.,  
27(5), 1153-8 (English) 1979. CODEN: CPBTAL. ISSN: 0009-2363.

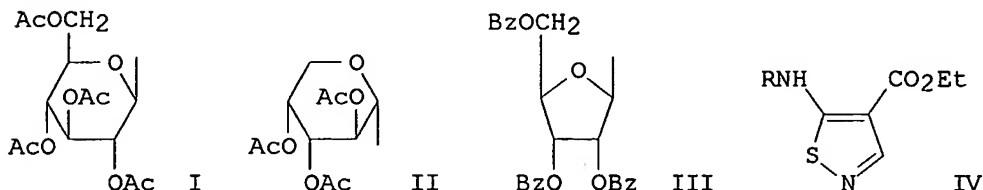
GI



AB Reactions of glycosyl isothiocyanates I, II, and III with  
o-phenylenediamine, 2,3-diaminopyridine or 5,6-diamino-1,3-dimethyluracil  
gave the corresponding glycosyl thioureides in good yields. Glycosyl  
thioureides were converted into nucleoside analogs IV, V, or VI (R =  
glycosyl) in excellent yields through a cyclodesulfurization reaction.

REFERENCE 2: 91:39764 Syntheses of nucleoside analogs using glycosyl isothiocyanate. Ogura, Haruo; Takahashi, Hiroshi (Sch. Pharm. Sci., Kitasato Univ., Tokyo, Japan). Tennen Yuki Kagobutsu Toronkai Koen Yoshishu, 21st, 221-8. Hokkaido Daigaku Nogakubo: Sapporo, Japan. (Japanese) 1978. CODEN: 39NQAF.

GI



AB Various nucleoside analogs contg. isothiazole, isothiazolopyrimidine, fused imidazole, pyrimidothiadiazine, pyrazolopyrimidine, triazole, or triazine moieties were prep'd. by using RNCS (R = I, II, or III). E.g., reaction of RNCS and MeC(NH<sub>2</sub>):CHCO<sub>2</sub>Et gave (glycosylamino)isothiazoles IV and MeC(NH<sub>2</sub>):C(SCNHR)CO<sub>2</sub>Et (V). V readily cyclized to IV.

REFERENCE 3: 84:150881 Modified nucleoside syntheses. Ogura, Haruo; Takahashi, Hiroshi; Takeda, Kazuyoshi; Sakaguchi, Masakazu; Nimura, Noriyuki; Sakai, Hitomi (Sch. Pharm. Sci., Kitasato Univ., Tokyo, Japan). Hukuskan Kagaku Toronkai Koen Yoshishu, 8th, 154-8. Pharm. Inst., Tohoku Univ.: Sendai, Japan. (Japanese) 1975. CODEN: 32KOAD.

GI For diagram(s), see printed CA Issue.

AB The isothiocyanates I and II were treated with o-C<sub>6</sub>H<sub>4</sub>(NH<sub>2</sub>)<sub>2</sub> or 5,6-diamino-1,3-dimethyluracil to give the modified nucleosides III and IV (X = CH:CHCH:CH, NMeCONMeCO, resp.). IV reacted with MeI with elimination of MeSH and gave the corresponding imidazoles V. R<sub>2</sub>COCH:C(NH<sub>2</sub>)NMeR<sub>3</sub> (R<sub>2</sub> = EtO, R<sub>3</sub> = Me; R<sub>2</sub>R<sub>3</sub> = NMeCONMe) reacted with I and II to give the corresponding pyrimidines (VI, VII, resp.).

L29 ANSWER 165 OF 177 REGISTRY COPYRIGHT 2002 ACS

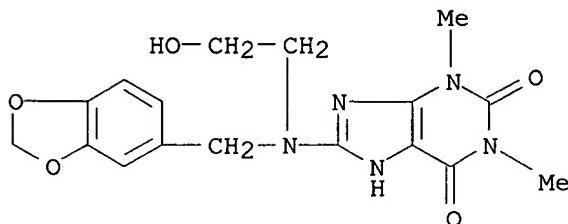
RN 40171-73-1 REGISTRY

CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)(2-hydroxyethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C17 H19 N5 O5

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 1E01

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 78:72181 8-Aminothephylline derivatives. (Laboratoire Lebrun S. A.). Fr. Demande FR 2116302 19720818, 15 pp. (French). CODEN: FRXXBL. APPLICATION: FR 1970-43891 19701207.

GI For diagram(s), see printed CA Issue.

AB 8-Aminothephyllines I ( $R =$  alkyl, aralkyl, hydroxyalkyl, chloroalkyl, aminoalkyl;  $R_1 =$  alkyl, aralkyl, aminoalkyl;  $NRR_1 =$  substituted piperazino, piperidino, pyrrolidino) (52 compds.) were prep'd. by treating 8-chlorothephylline or 8-bromotheophylline with  $RR_1NH$ . I displayed coronary dilator, diuretic, spasmolytic, and bronchodilator activities greater than that of theophylline, accompanied by lower toxicity.

L29 ANSWER 166 OF 177 REGISTRY COPYRIGHT 2002 ACS

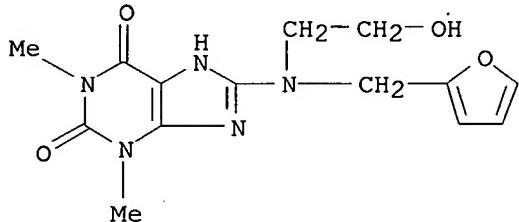
RN 40171-72-0 REGISTRY

CN 1H-Purine-2,6-dione, 8-[(2-furanyl methyl)(2-hydroxyethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C14 H17 N5 O4

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 78:72181 8-Aminothephylline derivatives. (Laboratoire Lebrun S. A.). Fr. Demande FR 2116302 19720818, 15 pp. (French). CODEN: FRXXBL. APPLICATION: FR 1970-43891 19701207.

GI For diagram(s), see printed CA Issue.

AB 8-Aminothephyllines I ( $R =$  alkyl, aralkyl, hydroxyalkyl, chloroalkyl, aminoalkyl;  $R_1 =$  alkyl, aralkyl, aminoalkyl;  $NRR_1 =$  substituted piperazino, piperidino, pyrrolidino) (52 compds.) were prep'd. by treating 8-chlorothephylline or 8-bromotheophylline with  $RR_1NH$ . I displayed coronary dilator, diuretic, spasmolytic, and bronchodilator activities greater than that of theophylline, accompanied by lower toxicity.

L29 ANSWER 167 OF 177 REGISTRY COPYRIGHT 2002 ACS

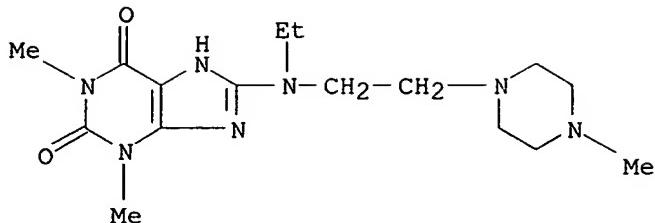
RN 40171-70-8 REGISTRY

CN 1H-Purine-2,6-dione, 8-[ethyl[2-(4-methyl-1-piperazinyl)ethyl]amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C16 H27 N7 O2

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 78:72181 8-Aminothephylline derivatives. (Laboratoire Lebrun S. A.). Fr. Demande FR 2116302 19720818, 15 pp. (French). CODEN: FRXXBL. APPLICATION: FR 1970-43891 19701207.

GI For diagram(s), see printed CA Issue.

AB 8-Aminothephyllines I (R = alkyl, aralkyl, hydroxyalkyl, chloroalkyl, aminoalkyl; R1 = alkyl, aralkyl, aminoalkyl; NR1 = substituted piperazino, piperidino, pyrrolidino) (52 compds.) were prep'd. by treating 8-chlorothephylline or 8-bromothephylline with RR1NH. I displayed coronary dilator, diuretic, spasmolytic, and bronchodilator activities greater than that of theophylline, accompanied by lower toxicity.

L29 ANSWER 168 OF 177 REGISTRY COPYRIGHT 2002 ACS

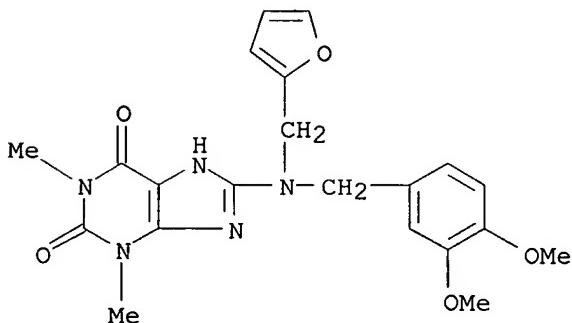
RN 40171-53-7 REGISTRY

CN 1H-Purine-2,6-dione, 8-[(3,4-dimethoxyphenyl)methyl](2-furanylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C21 H23 N5 O5

LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1962 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

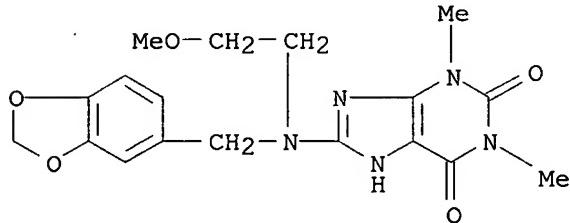
REFERENCE 1: 78:124636 Pharmacologically active 8-aminotheophylline derivatives. Laboratoire Lebrun S. A. (Laboratoire le Brun S. A.). Fr. Demande FR 2132582 19721229, 17 pp. (French). CODEN: FRXXBL. APPLICATION: FR 1971-12761 19710409.

GI For diagram(s), see printed CA Issue.  
AB The aminothiotheophyllines [I; X = S; R, R<sub>1</sub> = alkyl, alkoxyalkyl, hydroxyalkyl, aralkyl (92 compds.)], useful as spasmolytics, coronary dilators, antihitaminics, parasympatholytics, or antitussives, were prep'd. by treating the corresponding theophylline (I, X = O) with P2S5. Thus, I (X = O, R = R<sub>1</sub> = Et) was refluxed with P2S5 in dry pyridine to give 90% I (X = S, R = R<sub>1</sub> = Et).

REFERENCE 2: 78:72181 8-Aminothiotheophylline derivatives. (Laboratoire Lebrun S. A.). Fr. Demande FR 2116302 19720818, 15 pp. (French). CODEN: FRXXBL. APPLICATION: FR 1970-43891 19701207.

GI For diagram(s), see printed CA Issue.  
AB 8-Aminothiotheophyllines I (R = alkyl, aralkyl, hydroxyalkyl, chloroalkyl, aminoalkyl; R<sub>1</sub> = alkyl, aralkyl, aminoalkyl; NRR<sub>1</sub> = substituted piperazino, piperidino, pyrrolidino) (52 compds.) were prep'd. by treating 8-chlorothiotheophylline or 8-bromotheophylline with RR<sub>1</sub>NH. I displayed coronary dilator, diuretic, spasmolytic, and bronchodilator activities greater than that of theophylline, accompanied by lower toxicity.

L29 ANSWER 169 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 37136-09-7 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-2-ylmethyl)(2-methoxyethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C18 H21 N5 O5  
LC STN Files: BEILSTEIN\*, CA, CAPLUS  
(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1962 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

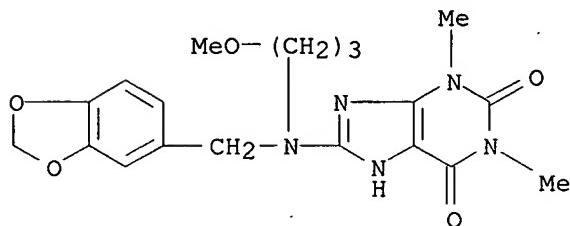
REFERENCE 1: 78:124636 Pharmacologically active 8-aminotheophylline derivatives. Laboratoire Lebrun S. A. (Laboratoire le Brun S. A.). Fr. Demande FR 2132582 19721229, 17 pp. (French). CODEN: FRXXBL. APPLICATION: FR 1971-12761 19710409.

GI For diagram(s), see printed CA Issue.  
AB The aminothiotheophyllines [I; X = S; R, R<sub>1</sub> = alkyl, alkoxyalkyl, hydroxyalkyl, aralkyl (92 compds.)], useful as spasmolytics, coronary dilators, antihitaminics, parasympatholytics, or antitussives, were prep'd. by treating the corresponding theophylline (I, X = O) with P2S5. Thus, I (X = O, R = R<sub>1</sub> = Et) was refluxed with P2S5 in dry pyridine to give 90% I (X = S, R = R<sub>1</sub> = Et).

REFERENCE 2: 77:101678 8-Aminothiotheophyllines. Laboratoire le Bruns S. A. Ger. Offen. DE 2160382 19720622, 26 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1971-2160382 19711206.

GI For diagram(s), see printed CA Issue.  
 AB About 110 title compds. [I, n = 2 or 3; R = H, Me, Et,  $(CH_2)_mOMe$  with m = 2 or 3,  $(CH_2)_m-OEt$ ,  $(CH_2)_mOH$ ,  $CH_2CH(OH)Me$ ,  $CH_2CH(OH)CH_2OH$ ,  $CH_2CH_2OPh$ ,  $CH_2CH_2OAc$ , 3,4-(OCH<sub>2</sub>O)C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>-nRn3 with R3 = H, p-Me, OMe, (OMe)<sub>2</sub>, 3,4,5-(OMe)3, p-Cl, Cl<sub>2</sub>, m-NO<sub>2</sub>, m-NH<sub>2</sub>, or p-OAc; R1 = Me, Et,  $CH_2CH_2OH$ , Ph, CHO, Ac, COEt, or Bz] were prepd. by reaction of 8-chlorotheophylline with amines RNH(CH<sub>2</sub>)<sub>n</sub>OR<sub>4</sub> (R<sub>4</sub> = H, Me, Et,  $CH_2CH_2OH$ , or Ph) and optional acylation. I were used as analgesics, antitussives, diuretics, antiinflammants, spasmolytics, coronary dilators, and bronchi dilators. The spasmolytic activity (ED<sub>50</sub> in mg/kg) of I [n = 2, R = 3,4-(OMe)2C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>, R1 = Ac] (II) in rabbit was 300, compared to 100 of papaverine, the coronary dilation by II in rabbit was 100, equiv. to theophylline, and the antitussive effect of II in guinea pigs was 110, equiv. to codeine.

L29 ANSWER 170 OF 177 REGISTRY COPYRIGHT 2002 ACS  
 RN 36750-50-2 REGISTRY  
 CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)(3-methoxypropyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C19 H23 N5 O5  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS  
 (\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1962 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 78:124636 Pharmacologically active 8-aminotheophylline derivatives. Laboratoire Lebrun S. A. (Laboratoire le Brun S. A.). Fr. Demande FR 2132582 19721229, 17 pp. (French). CODEN: FRXXBL.  
 APPLICATION: FR 1971-12761 19710409.

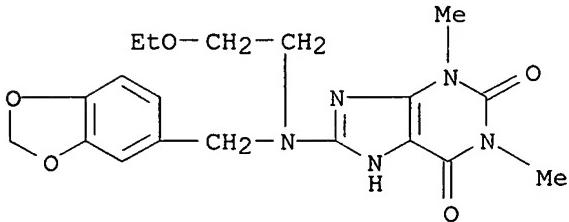
GI For diagram(s), see printed CA Issue.  
 AB The aminothiotheophyllines [I; X = S; R, R1 = alkyl, alkoxyalkyl, hydroxyalkyl, aralkyl (92 compds.)], useful as spasmolytics, coronary dilators, antihitaminics, parasympatholytics, or antitussives, were prepd. by treating the corresponding theophylline (I, X = O) with P2S5. Thus, I (X = O, R = R1 = Et) was refluxed with P2S5 in dry pyridine to give 90% I (X = S, R = R1 = Et).

REFERENCE 2: 77:101678 8-Aminothiotheophyllines. Laboratoire le Bruns S. A. Ger. Offen. DE 2160382 19720622, 26 pp. (German). CODEN: GWXXBX.  
 APPLICATION: DE 1971-2160382 19711206.

GI For diagram(s), see printed CA Issue.  
 AB About 110 title compds. [I, n = 2 or 3; R = H, Me, Et,  $(CH_2)_mOMe$  with m = 2 or 3,  $(CH_2)_m-OEt$ ,  $(CH_2)_mOH$ ,  $CH_2CH(OH)Me$ ,  $CH_2CH(OH)CH_2OH$ ,  $CH_2CH_2OPh$ ,  $CH_2CH_2OAc$ , 3,4-(OCH<sub>2</sub>O)C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>-nRn3 with R3 = H, p-Me, OMe,

(OMe)2, 3,4,5-(OMe)3, p-Cl, Cl2, m-NO2, m-NH2, or p-OAc; R1 = Me, Et, CH2CH2OH, Ph, CHO, Ac, COEt, or Bz] were prepd. by reaction of 8-chlorotheophylline with amines RNH(CH2)nOR4 (R4 = H, Me, Et, CH2CH2OH, or Ph) and optional acylation. I were used as analgesics, antitussives, diuretics, antiinflammants, spasmolytics, coronary dilators, and bronchi dilators. The spasmolytic activity (ED50 in mg/kg) of I [n = 2, R = 3,4-(OMe)2C6H3CH2, R1 = Ac] (II) in rabbit was 300, compared to 100 of papaverine, the coronary dilation by II in rabbit was 100, equiv. to theophylline, and the antitussive effect of II in guinea pigs was 110, equiv. to codeine.

L29 ANSWER 171 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 36750-44-4 REGISTRY  
CN 1H-Purine-2,6-dione, 8-[(1,3-benzodioxol-5-ylmethyl)(2-ethoxyethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C19 H23 N5 O5  
LC STN Files: BEILSTEIN\*, CA, CAPLUS  
(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1962 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 78:124636 Pharmacologically active 8-aminotheophylline derivatives. Laboratoire Lebrun S. A. (Laboratoire le Brun S. A.). Fr. Demande FR 2132582 19721229, 17 pp. (French). CODEN: FRXXBL.  
APPLICATION: FR 1971-12761 19710409.

GI For diagram(s), see printed CA Issue.  
AB The aminothiotheophyllines [I; X = S; R, R1 = alkyl, alkoxyalkyl, hydroxyalkyl, aralkyl (92 compds.)], useful as spasmolytics, coronary dilators, antihitaminics, parasympatholytics, or antitussives, were prepd. by treating the corresponding theophylline (I, X = O) with P2S5. Thus, I (X = O, R = R1 = Et) was refluxed with P2S5 in dry pyridine to give 90% I (X = S, R = R1 = Et).

REFERENCE 2: 77:101678 8-Aminotheophyllines. Laboratoire le Bruns S. A. Ger. Offen. DE 2160382 19720622, 26 pp. (German). CODEN: GWXXBX.  
APPLICATION: DE 1971-2160382 19711206.

GI For diagram(s), see printed CA Issue.  
AB About 110 title compds. [I, n = 2 or 3; R = H, Me, Et, (CH2)mOMe with m = 2 or 3, (CH2)m-OEt, (CH2)mOH, CH2CH(OH)Me, CH2CH(OH)CH2OH, CH2CH2OPh, CH2CH2OAc, 3,4-(OCH2O)C6H3CH2, CH2C6H5-nRn3 with R3 = H, p-Me, OMe, (OMe)2, 3,4,5-(OMe)3, p-Cl, Cl2, m-NO2, m-NH2, or p-OAc; R1 = Me, Et, CH2CH2OH, Ph, CHO, Ac, COEt, or Bz] were prepd. by reaction of 8-chlorotheophylline with amines RNH(CH2)nOR4 (R4 = H, Me, Et, CH2CH2OH, or Ph) and optional acylation. I were used as analgesics, antitussives,

diuretics, antiinflammants, spasmolytics, coronary dilators, and bronchi dilators. The spasmolytic activity (ED50 in mg/kg) of I [n = 2, R = 3,4-(OMe)2C6H3CH2, R1 = Ac] (II) in rabbit was 300, compared to 100 of papaverine, the coronary dilation by II in rabbit was 100, equiv. to theophylline, and the antitussive effect of II in guinea pigs was 110, equiv. to codeine.

L29 ANSWER 172 OF 177 REGISTRY COPYRIGHT 2002 ACS

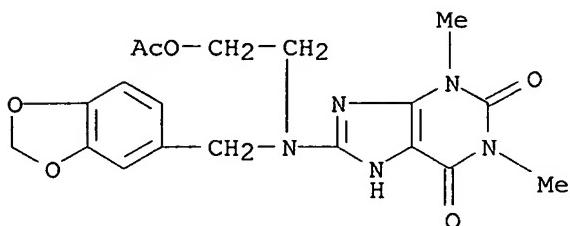
RN 36746-47-1 REGISTRY

CN 1H-Purine-2,6-dione, 8-[{2-(acetyloxy)ethyl}(1,3-benzodioxol-5-ylmethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H21 N5 O6

LC STN Files: CA, CAPLUS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 77:101678 8-Aminothephyllines. Laboratoire le Bruns S. A. Ger. Offen. DE 2160382 19720622, 26 pp. (German). CODEN: GWXXBX.

APPLICATION: DE 1971-2160382 19711206.

GI For diagram(s), see printed CA Issue.

AB About 110 title compds. [I, n = 2 or 3; R = H, Me, Et, (CH<sub>2</sub>)<sub>m</sub>OMe with m = 2 or 3, (CH<sub>2</sub>)<sub>m</sub>OEt, (CH<sub>2</sub>)<sub>m</sub>OH, CH<sub>2</sub>CH(OH)Me, CH<sub>2</sub>CH(OH)CH<sub>2</sub>OH, CH<sub>2</sub>CH<sub>2</sub>OPh, CH<sub>2</sub>CH<sub>2</sub>OAc, 3,4-(OCH<sub>2</sub>O)C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>-nRn3 with R3 = H, p-Me, OMe, (OMe)<sub>2</sub>, 3,4,5-(OMe)3, p-Cl, Cl<sub>2</sub>, m-NO<sub>2</sub>, m-NH<sub>2</sub>, or p-OAc; R1 = Me, Et, CH<sub>2</sub>CH<sub>2</sub>OH, Ph, CHO, Ac, COEt, or Bz] were prepd. by reaction of 8-chlorothephylline with amines RNH(CH<sub>2</sub>)<sub>n</sub>OR<sub>4</sub> (R<sub>4</sub> = H, Me, Et, CH<sub>2</sub>CH<sub>2</sub>OH, or Ph) and optional acylation. I were used as analgesics, antitussives, diuretics, antiinflammants, spasmolytics, coronary dilators, and bronchi dilators. The spasmolytic activity (ED50 in mg/kg) of I [n = 2, R = 3,4-(OMe)2C6H3CH2, R1 = Ac] (II) in rabbit was 300, compared to 100 of papaverine, the coronary dilation by II in rabbit was 100, equiv. to theophylline, and the antitussive effect of II in guinea pigs was 110, equiv. to codeine.

L29 ANSWER 173 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 33236-60-1 REGISTRY

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[{2-(1-piperidinyl)ethyl}amino]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Caffeine, 8-[{2-piperidinoethyl}amino]- (7CI, 8CI)

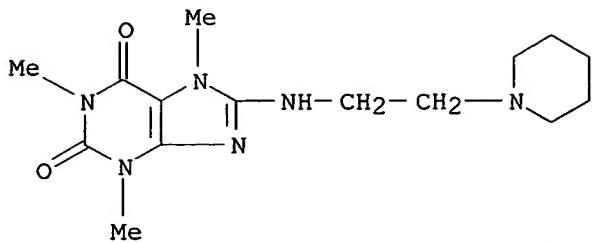
FS 3D CONCORD

MF C15 H24 N6 O2

CI COM

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS

(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1962 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 79:92274 Trisubstituted ethylenediamine derivatives.  
(Laboratorios Miquel S. A.). Span. ES 385302 19730416, 14 pp. (Spanish).  
CODEN: SPXXAD. APPLICATION: ES 1970-385302 19701022.

GI For diagram(s), see printed CA Issue.

AB Caffeine derivs. I (R = Me, Et, Pr, CHMe<sub>2</sub>, Bu, CH<sub>2</sub>CHMe<sub>2</sub>, cyclohexyl, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, 2-pyridyl, allyl; R<sub>1</sub> = 3,4-(MeO)C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>CHMe, PhCH<sub>2</sub>CHMe, PhCH(OH)CHMe, PhCH<sub>2</sub>CMe<sub>2</sub>, 3-HOC<sub>6</sub>H<sub>4</sub>CH(OH)CH<sub>2</sub>, PhCH<sub>2</sub>, PhCHMe, cyclohexyl, 2,2,3-trimethylbicyclo[2.2.1]hept-3-yl, Et, Pr, Bu, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, 3-pyridylmethyl; NRR<sub>1</sub> = morpholino, piperidino) were prep'd. by treating 8-chlorocaffeine with H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NRR<sub>1</sub>. I are central nervous system stimulants.

REFERENCE 2: 75:20324 Trisubstituted ethylenediamines. 1. Synthesis of trisubstituted ethylenediamines. Pitarch, L.; Iglesias, F.; Coronas, R. (Inst. Miquel Invest. Ter., Spain). Quim. Ind. (Madrid), 17(1), 71-6 (Spanish) 1971. CODEN: QUIBAL.

GI For diagram(s), see printed CA Issue.

AB I were prep'd. by reaction of 8-chlorocaffeine with amines or diamines. I has stimulant properties.

REFERENCE 3: 59:75376 8-Caffeinylalkylenediamines. Klosa, Josef (Delmar Chemicals Ltd.). US 3094529 19630618, 3 pp. (Unavailable). APPLICATION: US 19590911.

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) have a strong and sustained hypotensive action. Thus, 0.1 mole .beta.-(8-caffeinyl)aminoethyl chloride and 0.2 mole piperidine were refluxed with 40 ml. alc. 8 hrs. and cooled, the solid filtered off and dissolved in H<sub>2</sub>O, and the soln. made strongly alk. to give 1-piperidino-2-(8-caffeinyl)aminoethylene, m. 198-200.degree. (alc.); hydrochloride, m. 178-80.degree., 225-7.degree., and 268.degree. (decompn.). Similarly, prep'd. were I (R, n, R', and m.p. given): H, morpholino, 2, 181-3.degree. (alc.) (hydrochloride m. 220-2.degree.); dihydrochloride m. 170.degree. and 247-9.degree.); H, pyrrolidino, 3, 184-5.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether); H, NHPh, 3, 159-61.degree. (alc.); H, NHCHMeCH<sub>2</sub>Ph, 3, 163-5.degree. (alc.). By another method, 11 g. 8-chlorocaffeine was mixed with 8 ml. N-(hydroxyethyl)propylenediamine at 140-60.degree.; the temp. rose to 180.degree.. The mixt. was heated 0.5 hr., the solidified mass heated 10 min., cooled, and taken up in alc., an equal vol. H<sub>2</sub>O added, the soln. made strongly alk. the milky cloudiness solidified on cooling to give I (R = H, R<sub>1</sub> = NHCH<sub>2</sub>CH<sub>2</sub>OH, n = 3) m.

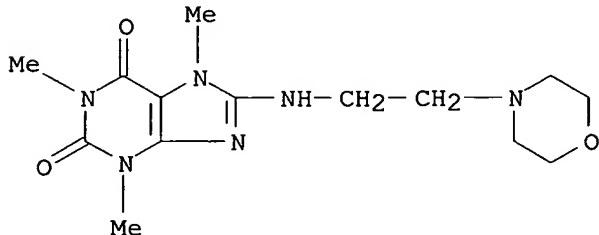
175-7.degree. (H<sub>2</sub>O). Similarly prep'd. were I (R, R', n, and m.p. given): H, NHCH<sub>2</sub>CH<sub>2</sub>OH, 2, 195-7.degree.; H, N(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>, 2, 142-4.degree..

REFERENCE 4: 58:33375 Caffeine-8-alkylene diamines. Klosa, Josef (Privat-Lab., Berlin Zehlendorf, Germany). J. Prakt. Chem., 18, 97-106 (Unavailable) 1962.

AB The title compds. were prep'd. by reaction of 8-chloro- or 8-bromocaffeine (I or II) and alkylendiamines or by treatment of 8-(.beta.-chloroalkyl)alkylamino- or aminocaffeine with primary or secondary bases. 8-(.beta.-Hydroxyethyl)aminocaffeine (10 g.) was added in portions to 10 ml. SOCl<sub>2</sub>, the mixt. heated 20-30 min. on a steam bath, and washed many times with refluxing C<sub>6</sub>H<sub>6</sub> to give 11 g. 8-(.beta.-chloroethyl)aminocaffeine (III), m. 225-7.degree. (MeOH). Similarly, 50 g. 8-(.gamma.-hydroxypropyl)amino-caffeine and 100 ml. SOCl<sub>2</sub>. gave 55 g. 8-(.beta.-chloropropyl)aminocaffeine (IV), m. 210-12.degree. (EtOH), and 40 g. 8-(.beta.-hydroxyethyl)-methylaminocaffeine and 40 ml. SOCl<sub>2</sub> refluxed 2 hrs. and then poured onto ice and neutralized with dil. NH<sub>3</sub> gave 8-(.beta.-chloroethyl)methylaminocaffeine (V). I (22 g.) and 23 g. Et<sub>2</sub>NCH<sub>2</sub>-CH<sub>2</sub>NH<sub>2</sub> were rubbed together, heated to 140.degree. to effect soln., and then refluxed 20 min. at 150-70.degree.. The mixt. was cooled, dissolved in hot EtOH, cooled, and filtered and the crystals dissolved in EtOH, treated with HCl-EtOH, and then with double the vol. of Et<sub>2</sub>O to give 80% N,N-diethyl-N'-(cafein-8-yl)ethylenediamine hydrochloride, m. 288-90.degree.; free base m. 186-8.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether); methobromide m. 230.degree.. I (44 g.) and 42 ml. Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>NH<sub>2</sub> heated a few min. at 160-70.degree. gave a mixt. which soon solidified and was purified by washing twice with refluxing EtOH, pptg. 80% N,N-diethyl-N'-(cafein-8-yl)trimethylenediamine hydrochloride, m. 222-4.degree. (Et-OH-Et<sub>2</sub>O); free base m. 158-60.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether or PhMe-petr. ether); methobromide m. 226.degree.; methiodide m. 244-6.degree. (MeOH). The following compds. were similarly prep'd. (product, % yield, m.p., crystn. solvent; hydrochloride m.p. given): N,N-dimethyl-N'-(cafein-8-yl)trimethylenediamine, 75-80, 173-5.degree., C<sub>6</sub>H<sub>6</sub>-petr. ether, 268-70.degree.; N-cyclohexyl-N'-(cafein-8-yl)-trimethylenediamine, --, 136-8.degree., C<sub>6</sub>H<sub>6</sub>-petr. ether, 240-2.degree. (dihydrochloride m. 240.degree.); N-methyl-N-(cafein-8-yl)-N',N'-diethylethylenediamine, --, 145-7.degree., --, --, N-ethyl-N-(cafein-8-yl)-N',N'-diethytethylenediamine, --, 138-40.degree., C<sub>6</sub>H<sub>6</sub>-petr. ether, --. V (28 g.), 10 ml. pyrrolidine, and 8 g. anhyd. K<sub>2</sub>CO<sub>3</sub> was refluxed 5-6 hrs. in 250 ml. 96% EtOH and the soln. filtered hot and reduced to half vol. to give 22 g. 1-(cafein-8-yl)methylamino-2-pyrrolidinoethane, m. 70-2.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether). The following compds. were similarly prep'd. from I, III, or IV and the appropriate amines (product, m.p., crystn. solvent, hydrochloride m.p. given): 1-piperidino-2-(cafein-8-yl)-ethane, 198-200.degree., EtOH, 268.degree. (decompn.); 1-morpholino-2-(cafein-8-yl)ethane, 181-3.degree., EtOH, 220-2.degree. [dihydrochloride m. 247-9.degree. (decompn.)]; N-benzyl-N'-(cafein-8-yl)ethylenediamine, --, --, 228-30.degree.; N,N-dibenzyl-N'-(cafein-8-yl)ethylenediamine, --, --, 195-7.degree.; N-isoamyl-N'-(cafein-8-yl)ethylenediamine, --, --, 223-5.degree.; 1-piperidino-3-(cafein-8-yl)aminopropane, 173-5.degree., C<sub>6</sub>H<sub>6</sub>-petr. ether, --; 1-pyrrolidino-3-(cafein-8-yl)aminopropane, 165-7.degree., C<sub>6</sub>H<sub>6</sub>-Petr. ether, --; N-phenyl-N'-(cafein-8-yl)trimethyl-enediamine, 159-61.degree., EtOH, --; N-(cafein-8-yl)-N'-(1-methylphenethyl)trimethylenediamine, 163-5.degree., EtOH, --; N-(cafein-8-yl)-N'-(1-hydroxyethyl)trimethylenediamine, 175-7.degree., H<sub>2</sub>O, --; N-(cafein-8-yl)-N',N'-bis(2-hydroxyethyl)ethylenediamine, 142-4.degree., EtOH, --; 8-(4-methylpiperazino)caffeine, 148-50.degree., PhMe-petr. ether, 344-6.degree. (methobromide m. 315-17.degree.; methiodide m. 314-16.degree.); salt between 8-hydroxycaffeine and N,N-

diethyltrimethylenediamine, 226.degree., EtOH.

L29 ANSWER 174 OF 177 REGISTRY COPYRIGHT 2002 ACS  
RN 33236-59-8 REGISTRY  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-(4-morpholinyl)ethyl)amino]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Caffeine, 8-[(2-morpholinoethyl)amino]- (7CI, 8CI)  
FS 3D CONCORD  
MF C14 H22 N6 O3  
LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS  
(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1962 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 79:92274 Trisubstituted ethylenediamine derivatives.  
(Laboratorios Miquel S. A.). Span. ES 385302 19730416, 14 pp. (Spanish).  
CODEN: SPXXAD. APPLICATION: ES 1970-385302 19701022.

GI For diagram(s), see printed CA Issue.

AB Caffeine derivs. I (R = Me, Et, Pr, CHMe<sub>2</sub>, Bu, CH<sub>2</sub>CHMe<sub>2</sub>, cyclohexyl, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, 2-pyridyl, allyl; R<sub>1</sub> = 3,4-(MeO)C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>CHMe, PhCH<sub>2</sub>CHMe, PhCH(OH)CHMe, PhCH<sub>2</sub>CMe<sub>2</sub>, 3-HOC<sub>6</sub>H<sub>4</sub>CH(OH)CH<sub>2</sub>, PhCH<sub>2</sub>, PhCHMe, cyclohexyl, 2,2,3-trimethylbicyclo[2.2.1]hept-3-yl, Et, Pr, Bu, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, 3-pyridylmethyl; NRR<sub>1</sub> = morpholino, piperidino) were prep'd. by treating 8-chlorocaffeine with H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NRR<sub>1</sub>. I are central nervous system stimulants.

REFERENCE 2: 75:20324 Trisubstituted ethylenediamines. 1. Synthesis of trisubstituted ethylenediamines. Pitarch, L.; Iglesias, F.; Coronas, R. (Inst. Miquel Invest. Ter., Spain). Quim. Ind. (Madrid), 17(1), 71-6 (Spanish) 1971. CODEN: QUIBAL.

GI For diagram(s), see printed CA Issue.

AB I were prep'd. by reaction of 8-chlorocaffeine with amines or diamines. I has stimulant properties.

REFERENCE 3: 59:75376 8-Caffeinylalkylenediamines. Klosa, Josef (Delmar Chemicals Ltd.). US 3094529 19630618, 3 pp. (Unavailable). APPLICATION: US 19590911.

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) have a strong and sustained hypotensive action. Thus, 0.1 mole .beta.- (8-caffeinyl)aminoethyl chloride and 0.2 mole piperidine were refluxed with 40 ml. alc. 8 hrs. and cooled, the solid filtered off and dissolved in H<sub>2</sub>O, and the soln. made strongly alk. to give 1-piperidino-2-(8-caffeinyl)aminoethylene, m. 198-200.degree. (alc.);

hydrochloride, m. 178-80.degree., 225-7.degree., and 268.degree. (decompn.). Similarly, prep'd. were I (R, n, R', and m.p. given): H, morpholino, 2, 181-3.degree. (alc.) (hydrochloride m. 220-2.degree.; dihydrochloride m. 170.degree. and 247-9.degree.); H, pyrrolidino, 3, 184-5.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether); H, NHPh, 3, 159-61.degree. (alc.); H, NHCHMeCH<sub>2</sub>Ph, 3, 163-5.degree. (alc.). By another method, 11 g. 8-chlorocaffeine was mixed with 8 ml. N-(hydroxyethyl)propylenediamine at 140-60.degree.; the temp. rose to 180.degree.. The mixt. was heated 0.5 hr., the solidified mass heated 10 min., cooled, and taken up in alc., an equal vol. H<sub>2</sub>O added, the soln. made strongly alk. the milky cloudiness solidified on cooling to give I (R = H, R<sub>1</sub> = NHCH<sub>2</sub>CH<sub>2</sub>OH, n = 3) m. 175-7.degree. (H<sub>2</sub>O). Similarly prep'd. were I (R, R', n, and m.p. given): H, NHCH<sub>2</sub>CH<sub>2</sub>OH, 2, 195-7.degree.; H, N(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>, 2, 142-4.degree..

REFERENCE 4: 58:33375 Caffeine-8-alkylene diamines. Klosa, Josef (Privat-Lab., Berlin Zehlendorf, Germany). J. Prakt. Chem., 18, 97-106 (Unavailable) 1962.

AB The title compds. were prep'd. by reaction of 8-chloro- or 8-bromocaffeine (I or II) and alkylendiamines or by treatment of 8-(.beta.-chloroalkyl)alkylamino- or aminocaffeine with primary or secondary bases. 8-(.beta.-Hydroxyethyl)aminocaffeine (10 g.) was added in portions to 10 ml. SOCl<sub>2</sub>, the mixt. heated 20-30 min. on a steam bath, and washed many times with refluxing C<sub>6</sub>H<sub>6</sub> to give 11 g. 8-(.beta.-chloroethyl)aminocaffeine (III), m. 225-7.degree. (MeOH). Similarly, 50 g. 8-(.gamma.-hydroxypropyl)amino-caffeine and 100 ml. SOCl<sub>2</sub>. gave 55 g. 8-(.beta.-chloropropyl)aminocaffeine (IV), m. 210-12.degree. (EtOH), and 40 g. 8-(.beta.-hydroxyethyl)-methylaminocaffeine and 40 ml. SOCl<sub>2</sub> refluxed 2 hrs. and then n<sub>2</sub>poured onto ice and neutralized with dil. NH<sub>3</sub> gave 8-(.beta.-chloroethyl)methylaminocaffeine (V). I (22 g.) and 23 g. Et<sub>2</sub>NCH<sub>2</sub>-CH<sub>2</sub>NH<sub>2</sub> were rubbed together, heated to 140.degree. to effect soln., and then refluxed 20 min. at 150-70.degree.. The mixt. was cooled, dissolved in hot EtOH, cooled, and filtered and the crystals dissolved in EtOH, treated with HCl-EtOH, and then with double the vol. of Et<sub>2</sub>O to give 80% N,N-diethyl-N'-(caffein-8-yl)ethylenediamine hydrochloride, m. 288-90.degree.; free base m. 186-8.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether); methobromide m. 230.degree.. I (44 g.) and 42 ml. Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>NH<sub>2</sub> heated a few min. at 160-70.degree. gave a mixt. which soon solidified and was purified by washing twice with refluxing EtOH, pptg. 80% N,N-diethyl-N'-(caffein-8-yl)trimethylenediamine hydrochloride, m. 222-4.degree. (Et-OH-Et<sub>2</sub>O); free base m. 158-60.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether or PhMe-petr. ether); methobromide m. 226.degree.; methiodide m. 244-6.degree. (MeOH). The following compds. were similarly prep'd. (product, % yield, m.p., crystn. solvent; hydrochloride m.p. given): N,N-dimethyl-N'-(caffein-8-yl)trimethylenediamine, 75-80, 173-5.degree., C<sub>6</sub>H<sub>6</sub>-petr. ether, 268-70.degree.; N-cyclohexyl-N'-(caffein-8-yl)-trimetnylenediamine, --, 136-8.degree., C<sub>6</sub>H<sub>6</sub>-petr. ether, 240-2.degree. (dihydrochloride m. 240.degree.); N-methyl-N-(caffein-8-yl)-N',N'-diethylethylenediamine, --, 145-7.degree., --, --, N-ethyl-N-(caffein-8-yl)-N',N'-diethytethylenediamine, --, 138-40.degree., C<sub>6</sub>H<sub>6</sub>-petr. ether, --. V (28 g.), 10 ml. pyrrolidine, and 8 g. anhyd. K<sub>2</sub>CO<sub>3</sub> was refluxed 5-6 hrs. in 250 ml. 96% EtOH and the soln. filtered hot and reduced to half vol. to give 22 g. 1-(caffein-8-yl)methylamino-2-pyrrolidinoethane, m. 70-2.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether). The following compds. were similarly prep'd. from I, III, or IV and the appropriate amines (product, m.p., crystn. solvent, hydrochloride m.p. given): 1-piperidino-2-(caffein-8-yl)-ethane, 198-200.degree., EtOH, 268.degree. (decompn.); 1-morpholino-2-(caffein-8-yl)ethane, 181-3.degree., EtOH, 220-2.degree. (dihydrochloride m. 247-9.degree. (decompn.)); N-benzyl-N'-(caffein-8-yl)ethylenediamine, --, --, 228-30.degree.; N,N-dibenzyl-N'-(caffein-8-yl)ethylenediamine, --, --, 195-7.degree.; N-isoamyl-N'-(caffein-8-

yl)ethylenediamine, --, --, 223-5.degree.; 1-piperidino-3-(cafein-8-yl)aminopropane, 173-5.degree., C6H6-petr. ether, --; 1-pyrrolidino-3-(cafein-8-yl)aminopropane, 165-7.degree., C6H6-Petr. ether, --; N-phenyl-N'-(cafein-8-yl)trimethyl-enediamine, 159-61.degree., EtOH, --; N-(cafein-8-yl)-N'-(1-methylphenethyl)trimethylenediamine, 163-5.degree., EtOH, --; N-(cafein-8-yl)-N'-(1-hydroxyethyl)trimethylenediamine, 175-7.degree., H2O, --; N-(cafein-8-yl)-N',N'-bis(2-hydroxyethyl)ethylenediamine, 142-4.degree., EtOH, --; 8-(4-methylpiperazino)caffeine, 148-50.degree., PhMe-petr. ether, 344-6.degree. (methobromide m. 315-17.degree.; methoiodide m. 314-16.degree.); salt between 8-hydroxycaffeine and N,N-diethyltrimethylenediamine, 226.degree., EtOH.

L29 ANSWER 175 OF 177 REGISTRY COPYRIGHT 2002 ACS

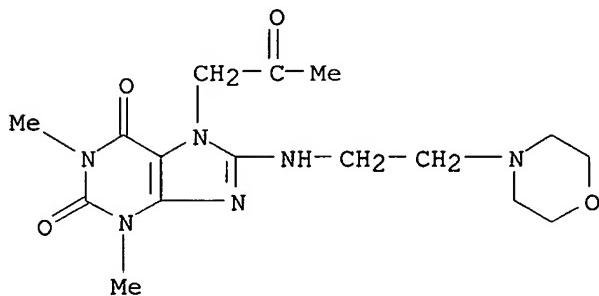
RN 1051-26-9 REGISTRY

CN Theophylline, 7-acetonyl-8-[(2-morpholinoethyl)amino]-, monohydrochloride (8CI) (CA INDEX NAME)

MF C16 H24 N6 O4 . Cl H

LC STN Files: CAOLD

CRN (979-53-3)



● HCl

#### 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L29 ANSWER 176 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 979-53-3 REGISTRY

CN Theophylline, 7-acetonyl-8-[(2-morpholinoethyl)amino]- (7CI, 8CI) (CA INDEX NAME)

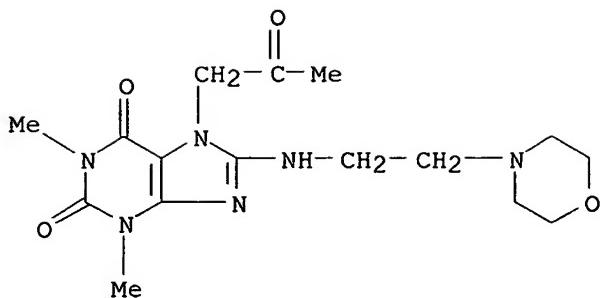
FS 3D CONCORD

MF C16 H24 N6 O4

CI COM

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS

(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 62:51641 Synthesis in the theophylline series. XI. Synthesis of 7-acetonyltheophyllines. J. Prakt. Chem., 26(3-4), 155-8 (Unavailable) 1964.

AB I or the Br analog with dialkylaminoalkylamines yielded the corresponding II under mild conditions. I (27 g.) and 11.6 g. Et<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> in 100 cc. iso-PrOH refluxed 5 hrs. yielded 25 g. II (R = H, R<sub>1</sub> = CH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>) (V), m. 143-5.degree. (repptd. from MePh with petr. ether); V. HCl m. 288-90.degree.; V. MeBr m. 297-9.degree.. Similarly were prep'd. the following II (R, R<sub>1</sub>, and m.ps. of base and HCl salt given): H, Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>, 118-20.degree., 260-2.degree. (methobromide m. 238-40.degree.); H, Me<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>, 125-7.degree., 240-2.degree. (methobromide m. 225-7.degree.); Me, Et<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>, 98, -- (hygroscopic); Me, Me<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>, 114-16.degree., 254-6.degree.; H, 2-piperidinoethyl, 158-60.degree., --; H, 2-morpholinoethyl, 198-200.degree., 266-8.degree.; H, 3-cyclohexylaminopropyl, 120-2.degree., 325-7.degree.. Similarly was prep'd. II [(R<sub>1</sub> = ) 4-methylpiperazino)], m. 135-7.degree.; HCl salt m. 272-4.degree.. II did not reach the pharmacol. activity of theophylline, caffeine, or 7-acetonyltheophylline.

L29 ANSWER 177 OF 177 REGISTRY COPYRIGHT 2002 ACS

RN 979-52-2 REGISTRY

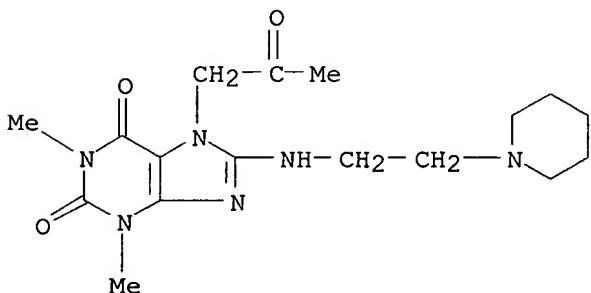
CN Theophylline, 7-acetonyl-8-[(2-piperidinoethyl)amino]- (7CI, 8CI) (CA INDEX NAME)

FS 3D CONCORD

MF C17 H26 N6 O3

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS

(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1962 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 62:51641 Synthesis in the theophylline series. XI. Synthesis of 7-acetonyltheophyllines. J. Prakt. Chem., 26(3-4), 155-8 (Unavailable) 1964.

AB I or the Br analog with dialkylaminoalkylamines yielded the corresponding II under mild conditions. I (27 g.) and 11.6 g. Et<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> in 100 cc. iso-PrOH refluxed 5 hrs. yielded 25 g. II (R = H, R<sub>1</sub> = CH<sub>2</sub>CH<sub>2</sub>NEt<sub>2</sub>) (V), m. 143-5.degree. (repptd. from MePh with petr. ether); V. HCl m. 288-90.degree.; V. MeBr m. 297-9.degree.. Similarly were prep'd. the following II (R, R<sub>1</sub>, and m.ps. of base and HCl salt given): H, Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>, 118-20.degree., 260-2.degree. (methobromide m. 238-40.degree.); H, Me<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>, 125-7.degree., 240-2.degree. (methobromide m. 225-7.degree.); Me, Et<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>, 98, -- (hygroscopic); Me, Me<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>, 114-16.degree., 254-6.degree.; H, 2-piperidinoethyl, 158-60.degree., --; H, 2-morpholinoethyl, 198-200.degree., 266-8.degree.; H, 3-cyclohexylaminopropyl, 120-2.degree., 325-7.degree.. Similarly was prep'd. II [(R<sub>1</sub> = ) 4-methylpiperazino)], m. 135-7.degree.; HCl salt m. 272-4.degree.. II did not reach the pharmacol. activity of theophylline, caffeine, or 7-acetonyltheophylline.

=> dis his

(FILE 'HOME' ENTERED AT 13:33:05 ON 03 DEC 2002)

FILE 'REGISTRY' ENTERED AT 13:33:13 ON 03 DEC 2002

L1 STR  
L2 50 S L1  
L3 5409 S L1 FUL  
L4 STR L1  
L5 80 SEARCH L4 SUB=L3 FUL  
L6 STR L4  
L7 0 SEARCH L6 SUB=L5 FUL  
L9 51 SEARCH L\*\*\* SUB=L5 FUL  
L10 STR L\*\*\*  
L11 5 SEARCH L10 SUB=L9 FUL  
L12 STR L5  
L13 0 SEARCH L12 SUB=L5 FUL  
L14 STR L12  
L15 0 SEARCH L14 SUB=L5 FUL  
L16 STR L14  
L17 0 SEARCH L16 SUB=L5 FUL  
L18 35 S L15  
L19 50 S L16  
L20 STR L16  
L21 0 SEARCH L20 SUB=L5 FUL  
L22 249 SEARCH L20 SUB=L3 FUL

FILE 'HCAPLUS' ENTERED AT 13:57:58 ON 03 DEC 2002

L23 36 S L22

FILE 'REGISTRY' ENTERED AT 13:58:51 ON 03 DEC 2002

L24 STR L1

```
L25      7 SEARCH L24  SUB=L3 FUL
L26      STR L1
L27      0 SEARCH L26  SUB=L3 FUL
L28      STR L1
L29      177 SEARCH L28  SUB=L3 FUL
```

=> save l3 berch/a

'BERCH/A' IN USE

A single name cannot be used for two saved items at the same time.  
Enter "Y" if you wish to replace the current saved name with a new  
definition. Enter "N" if the current saved definition must be  
preserved. You may then reenter the SAVE command with a different  
saved name. Enter "DISPLAY SAVED" at an arrow prompt (=>) to see a  
list of your currently defined saved names.

REPLACE OLD DEFINITION? Y/(N):y

ANSWER SET L3 HAS BEEN SAVED AS 'BERCH/A'

=> log y

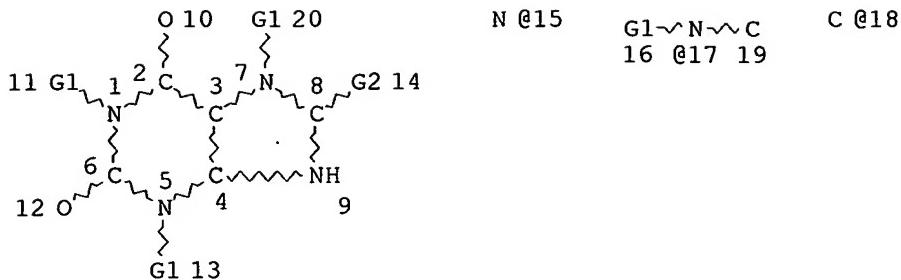
COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
----------------------	------------------	---------------

FULL ESTIMATED COST	524.47	1216.56
---------------------	--------	---------

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
--	------------------	---------------

CA SUBSCRIBER PRICE	-35.40	-59.47
---------------------	--------	--------

STN INTERNATIONAL LOGOFF AT 14:05:06 ON 03 DEC 2002



```

VAR G1=H/C
VAR G2=15/17/18
NODE ATTRIBUTES:
NSPEC IS R AT 15
NSPEC IS RC AT 18
NSPEC IS RC AT 19
CONNECT IS M1 RC AT 10
CONNECT IS M1 RC AT 12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

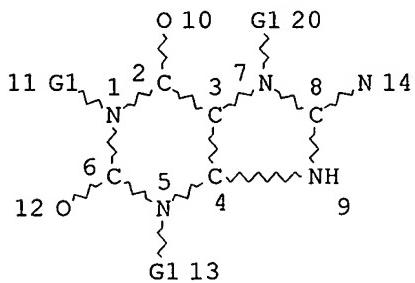
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

```

```

STEREO ATTRIBUTES: NONE
L3 5409 SEA FILE=REGISTRY SSS FUL L1
L4 STR

```



```

VAR G1=H/C
NODE ATTRIBUTES:
NSPEC IS R AT 14
CONNECT IS M1 RC AT 10
CONNECT IS M1 RC AT 12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

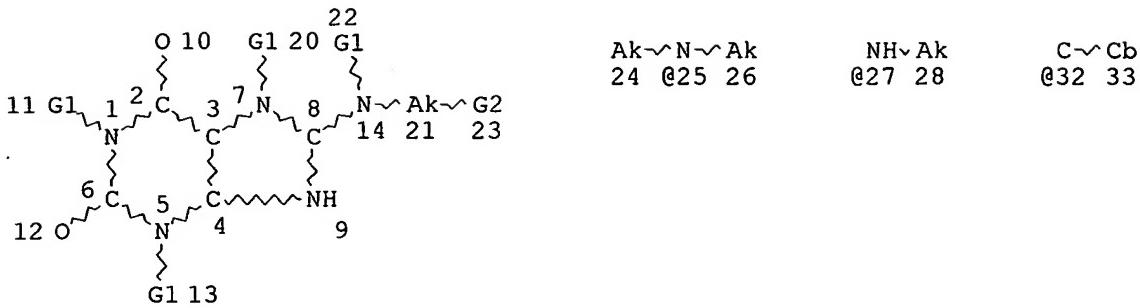
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

```

```

STEREO ATTRIBUTES: NONE
L5 80 SEA FILE=REGISTRY SUB=L3 SSS FUL L4
L14 STR

```



C~C~Cb  
@29 30 31      C~G3~Hy  
@34 35 36

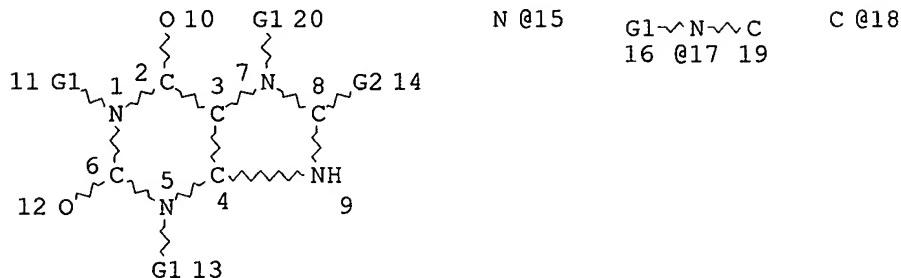
VAR G1=H/C  
 VAR G2=NH2/25/27/32/29/HY/34/CB  
 REP G3=(0-1) C  
 NODE ATTRIBUTES:  
 CONNECT IS M1 RC AT 10  
 CONNECT IS M1 RC AT 12  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE  
 L15      0 SEA FILE=REGISTRY SUB=L5 SSS FUL L14

100.0% PROCESSED      80 ITERATIONS      0 ANSWERS  
 SEARCH TIME: 00.00.01

=> d 122 que stat;fil hcaplus;s 122  
 L1      STR

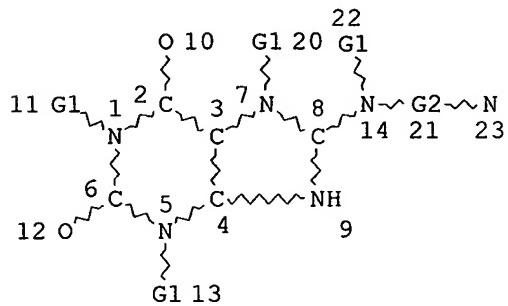


VAR G1=H/C  
 VAR G2=15/17/18  
 NODE ATTRIBUTES:  
 NSPEC      IS R      AT 15  
 NSPEC      IS RC      AT 18  
 NSPEC      IS RC      AT 19

CONNECT IS M1 RC AT 10  
CONNECT IS M1 RC AT 12  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE  
L3 5409 SEA FILE=REGISTRY SSS FUL L1  
L20 STR



VAR G1=H/C  
REP G2=(1-4) C  
NODE ATTRIBUTES:  
CONNECT IS M1 RC AT 10  
CONNECT IS M1 RC AT 12  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE  
L22 249 SEA FILE=REGISTRY SUB=L3 SSS FUL L20

100.0% PROCESSED 348 ITERATIONS 249 ANSWERS  
SEARCH TIME: 00.00.01

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	533.47	533.68
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.77	-1.77

FILE 'HCAPLUS' ENTERED AT 13:57:58 ON 03 DEC 2002  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 3 Dec 2002 VOL 137 ISS 23  
FILE LAST UPDATED: 2 Dec 2002 (20021202/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

L23 36 L22

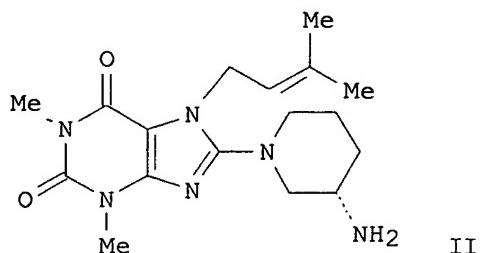
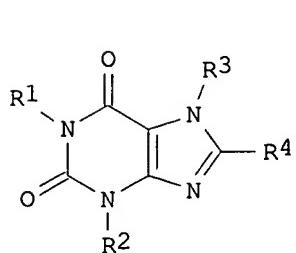
36 L22

=> d 1-36 cbib abs hitstr

L23 ANSWER 1 OF 36 HCAPLUS COPYRIGHT 2002 ACS

2002:676018 Document No. 137:216824 Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1 20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE 2002-10203486 20020130.

GI



AB Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the

dipeptidylpeptidase-IV enzyme. Pharmaceutical compns. contg. I are described. Thus, II was prep'd. and had an IC<sub>50</sub> of 22 nM against dipeptidylpeptidase-IV.

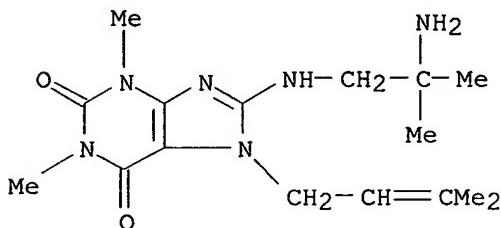
IT 454707-01-8P 454707-02-9P 454707-03-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of xanthine derivs. as dipeptidylpeptidase-IV inhibitors)

RN 454707-01-8 HCAPLUS

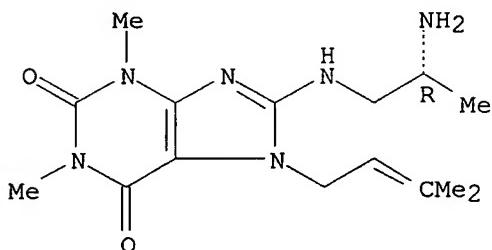
CN 1H-Purine-2,6-dione, 8-[(2-amino-2-methylpropyl)amino]-3,7-dihydro-1,3-dimethyl-7-(3-methyl-2-but enyl)- (9CI) (CA INDEX NAME)



RN 454707-02-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2R)-2-aminopropyl]amino]-3,7-dihydro-1,3-dimethyl-7-(3-methyl-2-but enyl)- (9CI) (CA INDEX NAME)

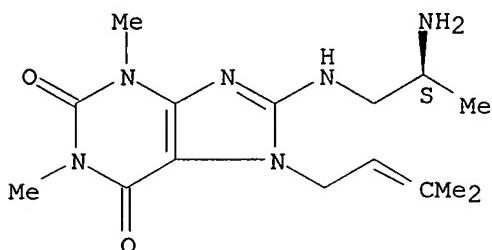
Absolute stereochemistry.



RN 454707-03-0 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2S)-2-aminopropyl]amino]-3,7-dihydro-1,3-dimethyl-7-(3-methyl-2-but enyl)- (9CI) (CA INDEX NAME)

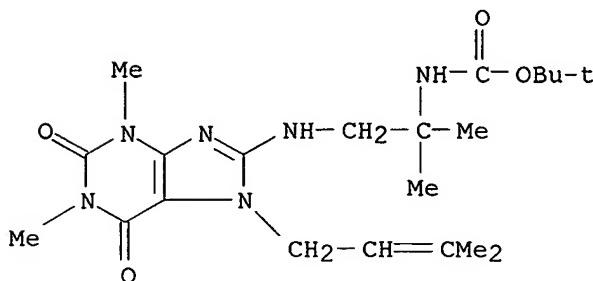
Absolute stereochemistry.



IT 454709-97-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prep. of xanthine derivs. as dipeptidylpeptidase-IV inhibitors)  
RN 454709-97-8 HCAPLUS  
CN Carbamic acid, [1,1-dimethyl-2-[(2,3,6,7-tetrahydro-1,3-dimethyl-7-(3-methyl-2-butenoxy)-2,6-dioxo-1H-purin-8-yl)amino]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



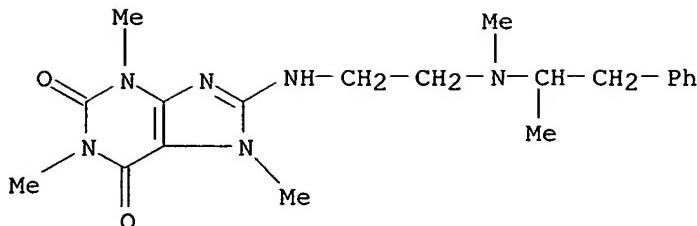
L23 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2002 ACS

2002:288083 Document No. 137:272615 Toxicokinetics of amphetamines: metabolism and toxicokinetic data of designer drugs, amphetamine, methamphetamine, and their N-alkyl derivatives. Kraemer, Thomas; Maurer, Hans H. (Department of Experimental and Clinical Toxicology, University of Saarland, Homburg, Germany). Therapeutic Drug Monitoring, 24(2), 277-289 (English) 2002. CODEN: TDMODV. ISSN: 0163-4356. Publisher: Lippincott Williams & Wilkins.

AB A review. This paper reviews the toxicokinetics of amphetamines. The designer drugs MDA (methylenedioxy-amphetamine, R,S-1-(3',4'-methylenedioxyphenyl)-2-propanamine), MDMA (R,S-methylenedioxymethamphetamine), and MDE (R,S-methylenedioxymethylamphetamine), as well as BDB (benzodioxolylbutanamine; R,S-1-(1',3'-benzodioxol-5'-yl)-2-butanamine or R,S-1-(3',4'-methylenedioxyphenyl)-2-butanamine) and MBDB (R,S-N-methyl-benzodioxolylbutanamine), were taken into consideration, as were the following N-alkylated amphetamine derivs.: amphetamine, benzphetamine, clobenzorex, dimethylamphetamine, ethylamphetamine, famprofazone, fencamine, fenethylline, fenproporex, furfenorex, mefenorex, mesocarb, methamphetamine, pencytamine, and selegiline. English-language publications from 1995 to 2000 were reviewed. Papers describing identification of metabolites or cytochrome P 450 isoenzyme-dependent metab. and papers contg. pharmacokinetic/toxicokinetic data were considered and summarized. The implications of toxicokinetics for toxicol. assessment or for interpretation in forensic cases are discussed.

IT 28947-50-4, Fencamine  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(toxicokinetics of amphetamine, methamphetamine, and their N-alkyl derivs.)

RN 28947-50-4 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[[2-[methyl(1-methyl-2-phenylethyl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)



L23 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2002 ACS

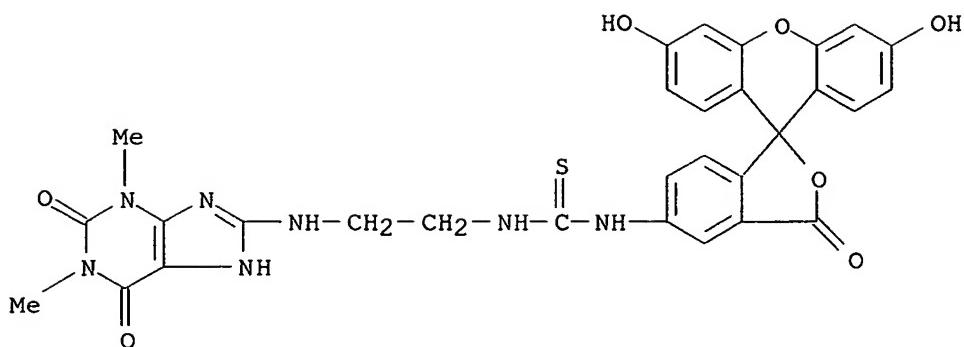
1996:401614 Document No. 125:53030 Compositions and methods for use in detection of analytes. Reddy, M. Parameswara; Sternberg, James C. (Beckman Instruments, Inc., USA). PCT Int. Appl. WO 9606948 A1 19960307, 59 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US10226 19950810. PRIORITY: US 1994-298523 19940830.

AB Double-stranded nucleic acid duplexes serve as universal harvestable and cleavable link systems in a variety of different types of immunoassays (e.g., sandwich, competitive, etc.). Depending upon the type of assay, at least one specific component involved in the assay system is attached to a first member of a pair of sequences forming a double-stranded nucleic acid (i.e., two oligonucleotides comprising substantially complementary sequences). The assay is carried out in the presence of a support to which is attached an oligonucleotide which is the other member of the pair of sequences forming a double-stranded nucleic acid duplex under hybridization conditions. Upon the hybridization of the two complementary oligonucleotides to form a duplex, the component of the assay system to which the first member of the pair of oligonucleotides is attached may thereby be effectively removed from the soln. phase and harvested onto the support. Oligonucleotides bound to a support are reusable in multiple successive assays. Moreover, any given support-bound oligonucleotide can be used in accordance with the present invention for the anal. of a variety of different analytes. In many cases, the assay system includes a label to facilitate quantifying the amt. of analyte; in others, the amt. of analyte may be detd. without the use of any extraneous label. Examples show the detn. of phenobarbital, theophylline, and TSH and combinations of 2 or all 3 of them.

IT 178318-54-2P  
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)  
 (double-stranded nucleic acids as universal link system in immunoassays)

RN 178318-54-2 HCAPLUS

CN Thiourea, N-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)-N'-(2-[(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)amino]ethyl)- (9CI) (CA INDEX NAME)



L23 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1996:183066 Document No. 124:278873 Synthesis, toxicological and pharmacological investigations of 8-basic substituted derivatives of caffeine. Danchev, N.; Zlatkov, A.; Peikov, P. (Dep. Pharmacol., Faculty Pharmacy, Sofia, Bulg.). Dokladi na Bulgarskata Akademiya na Naukite, 48(5), 119-22 (English) 1995. CODEN: DBANEH. ISSN: 0861-1459. Publisher: Izdatelstvo na Bulgarskata Akademiya na Naukite.

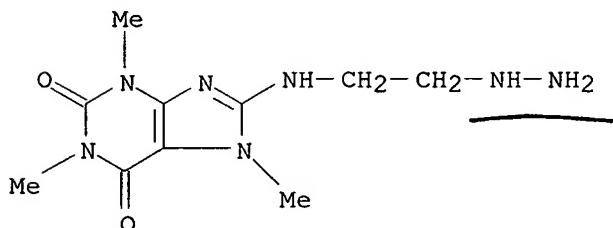
AB The prepn. of some new 8-basic substituted derivs. of caffeine and their psychostimulant, hypotensive, antiarrhythmic activity and toxicity is reported.

IT 137018-92-9P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and psychostimulant, hypotensive, antiarrhythmic activity and toxicity of 8-basic substituted caffeine derivs.)

RN 137018-92-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-hydrazinoethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



IT 136611-59-1P 175735-02-1P 175735-03-2P

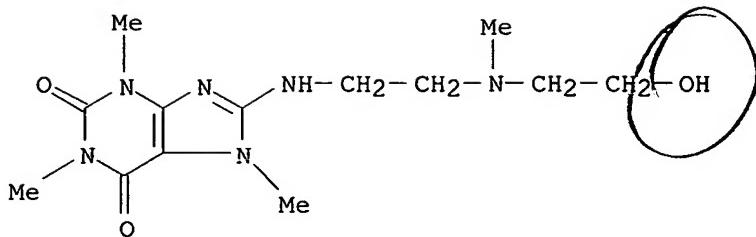
175735-04-3P 175735-05-4P 175735-06-5P

175735-07-6P 175735-08-7P 175735-09-8P

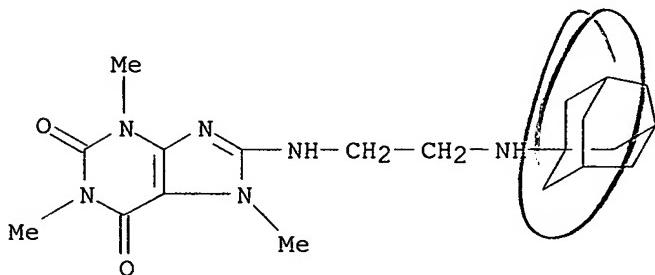
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and psychostimulant, hypotensive, antiarrhythmic activity and toxicity of 8-basic substituted caffeine derivs.)

RN 136611-59-1 HCAPLUS

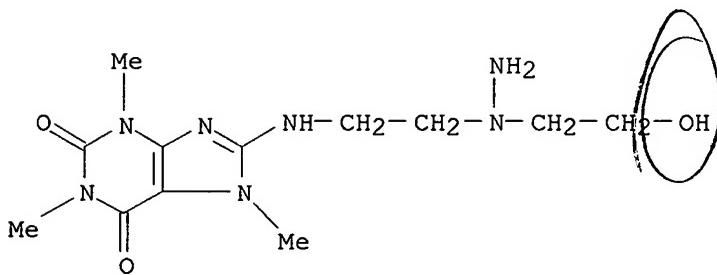
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[[2-[(2-hydroxyethyl)methylamino]ethyl]amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



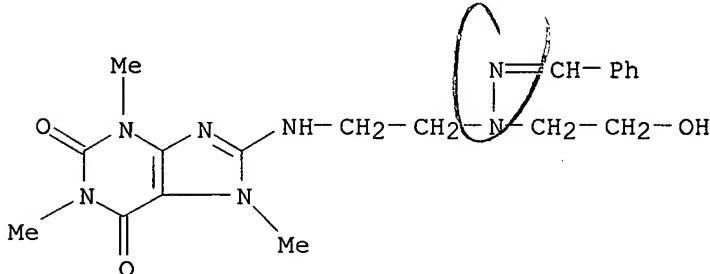
RN 175735-02-1 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-(tricyclo[3.3.1.13,7]dec-1-ylamino)ethyl)amino]- (9CI) (CA INDEX NAME)



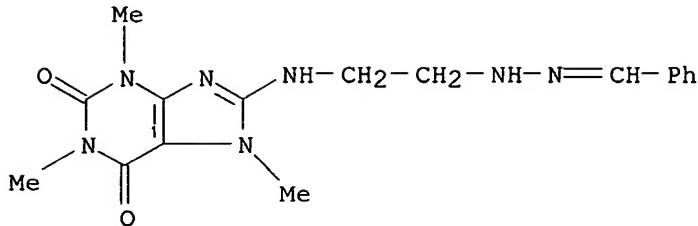
RN 175735-03-2 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(2-[1-(2-hydroxyethyl)hydrazino]ethyl)amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 175735-04-3 HCAPLUS  
 CN Benzaldehyde, (2-hydroxyethyl)[2-[(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)amino]ethyl]hydrazone (9CI) (CA INDEX NAME)

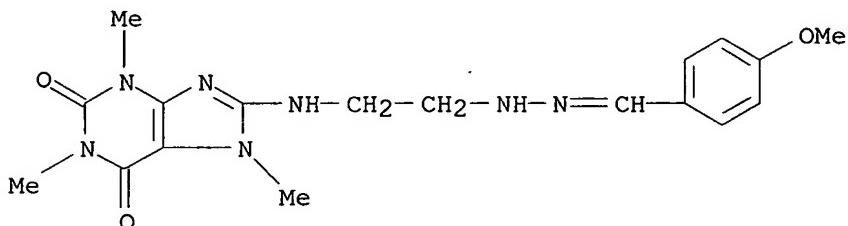


RN 175735-05-4 HCAPLUS  
 CN Benzaldehyde, [2-[(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)amino]ethyl]hydrazone (9CI) (CA INDEX NAME)



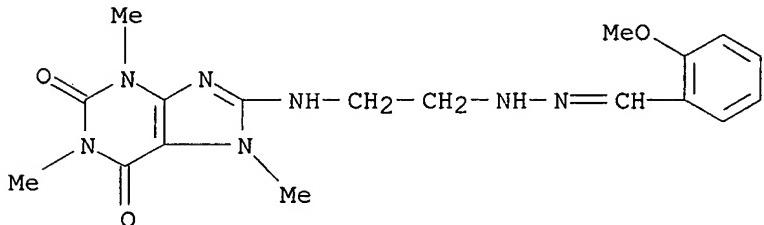
RN 175735-06-5 HCAPLUS

CN Benzaldehyde, 4-methoxy-, [2-[(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)amino]ethyl]hydrazone (9CI) (CA INDEX NAME)



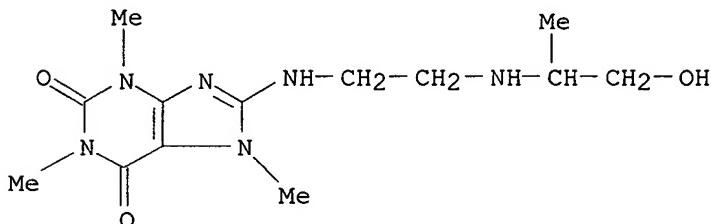
RN 175735-07-6 HCAPLUS

CN Benzaldehyde, 2-methoxy-, [2-[(2,3,6,7-tetrahydro-1,3,7-trimethyl-2,6-dioxo-1H-purin-8-yl)amino]ethyl]hydrazone (9CI) (CA INDEX NAME)



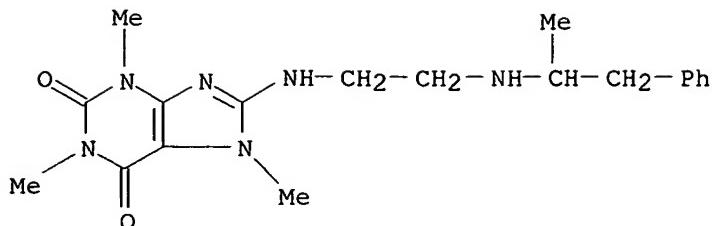
RN 175735-08-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[[2-[(2-hydroxy-1-methylethyl)amino]ethyl]amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 175735-09-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[(1-methyl-2-phenylethyl)amino]ethyl)amino]- (9CI) (CA INDEX NAME)



L23 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1995:560596 Document No. 122:309889 Potential bioreductively activated hypoxia probes and post-irradiation radiosensitizers related to NITP. Mehta, Lina K.; Monney, Hugh; Parrick, John; Hodgkiss, Richard J. (Chem. Dep., Brunel Univ., Middlesex, UB8 3PH, UK).. Anti-Cancer Drug Design, 10(3), 227-41 (English) 1995. CODEN: ACDDEA. ISSN: 0266-9536.

Publisher: Oxford University Press.

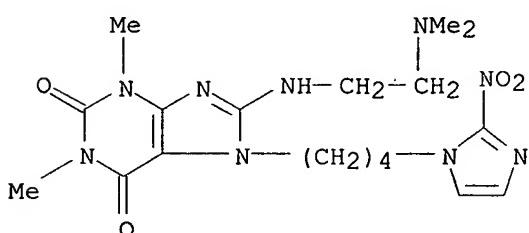
AB NITP (1) is an effective marker of hypoxia in tumors for both microscopy and cell sorting studies and, addnl., the compd. shows postirradn. sensitization, probably by inhibition of repair of radiation damage to DNA. However, NITP does not have the substitution pattern which the immunochem. reagents are raised to recognize and the compd. has very low solv. in water. We report the synthesis of an isomer (13) of NITP which has the desirable substitution pattern and is also sol. in very weak aq. base. The successful synthesis of 13 uses a nitrosation and cyclization of a substituted uracil (16), but earlier approaches from 5 and 12 yielded the pyridoxanthine deriv. 6. The preparative use of nitro group displacement reactions from 8-nitrocaffeine is shown to be a useful entry to a range of 8-substituted caffelines and is utilized to obtain two derivs. of NITP which carry aliph. amine chains, i.e., 34 and 35.

IT 163436-04-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (potential bioreductively activated hypoxia probes and radiosensitizers related to NITP)

RN 163436-04-2 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[[2-(dimethylamino)ethyl]amino]-3,7-dihydro-1,3-dimethyl-7-[4-(2-nitro-1H-imidazol-1-yl)butyl] (9CI) (CA INDEX NAME)



L23 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1995:257491 Document No. 122:105801 Synthesis and physicochemical properties of novel basic substituted methylxanthine derivatives. Zlatkov, Alexander; Peikov, Plamen; Yamboliev, Ilia (Fac. Pharmacy, Sofia, 1000, Bulg.). Pharmakeutike, 7(2), 79-84 (English) 1994. CODEN: PHMKE4. ISSN: 1105-4999. Publisher: Pharmaceutical Publications.

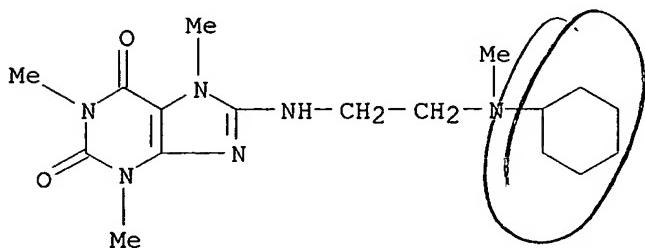
AB Novel, basic, side-chain-contg. compds. with possible biol. activity were synthesized by N-alkylation of N-methylcyclohexylamine with different halo- and (haloalkyl)methylxanthines. UV-absorption spectra, water solv., and n-octanol/water partition behavior were recorded. Compared to natural methylxanthines, a higher water solv. was achieved, which, along with the absorption spectra, was poorly pH-dependent.

IT 160726-52-3P 160726-54-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of)

RN 160726-52-3 HCAPLUS

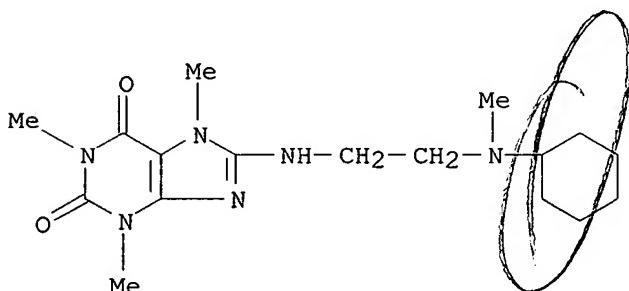
CN 1H-Purine-2,6-dione, 8-[(2-(cyclohexylmethylamino)ethyl]amino]-3,7-dihydro-1,3,7-trimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 160726-54-5 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-(cyclohexylmethylamino)ethyl]amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



L23 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1994:128315 Document No. 120:128315 Inhibition of Cyclic Nucleotide Phosphodiesterase by Derivatives of 1,3-Bis(cyclopropylmethyl)xanthine.  
Buckle, Derek R.; Arch, Jonathan R. S.; Connolly, Brendan J.; Fenwick, Ashley E.; Foster, Keith A.; Murray, Kenneth J.; Readshaw, Simon A.; Smallridge, Mark; Smith, David G. (SmithKline Beecham Pharmaceuticals, Epsom/Surrey, KT18 5XQ, UK). Journal of Medicinal Chemistry, 37(4), 476-85 (English) 1994. CODEN: JMCMAR. ISSN: 0022-2623.

AB Alkylation of the selective type IV phosphodiesterase inhibitor, 8-amino-1,3-bis(cyclopropylmethyl)xanthine (I, BRL 61063), led exclusively to the N-7 substituted derivs., which showed varying selectivities for the PDE type IV isoenzyme relative to PDE Va. The 4-methoxybenzyl deriv. in particular was a highly potent PDE Va inhibitor ( $IC_{50}$  0.14  $\mu$ M) and showed a 24-fold selectivity for this isoenzyme relative to PDE IV. Sulfonation of I was more complex, with the product profile being highly

dependent on the reaction conditions. As with alkylation, sulfonation at N-7 generally increased potency against PDE Va, esp. in the aryl-contg. moieties lacking strongly electron-withdrawing substituents. Bis-arylsulfonation at the exocyclic amino group generally reduced inhibitory potency against both PDE IV and Va. An 8-amidino compd., formed by the unusual reaction of I with N-methylpyrrolidinone in the presence of benzenesulfonyl chloride, had an IC<sub>50</sub> value of 0.05 .μ.M against PDE Va and is believed to be the most potent inhibitor of this isoenzyme reported. No correlation of PDE IV inhibition with displacement of [<sup>3</sup>H]rolipram from its high-affinity binding site was demonstrated. This suggests that either the catalytic site and the rolipram binding site are not the same or that PDE IV can exist in two conformations, only one of which binds to rolipram with high affinity, and that the compds. described vary in their selectivity for this isoform.

IT

153284-16-3P

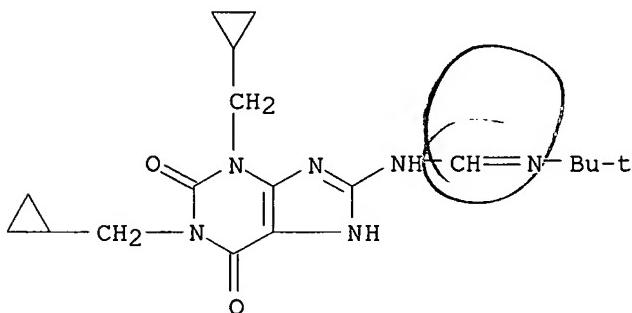
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and cyclic nucleotide phosphodiesterase isoenzymes inhibition  
by, structure in relation to)

RN

153284-16-3 HCAPLUS

CN

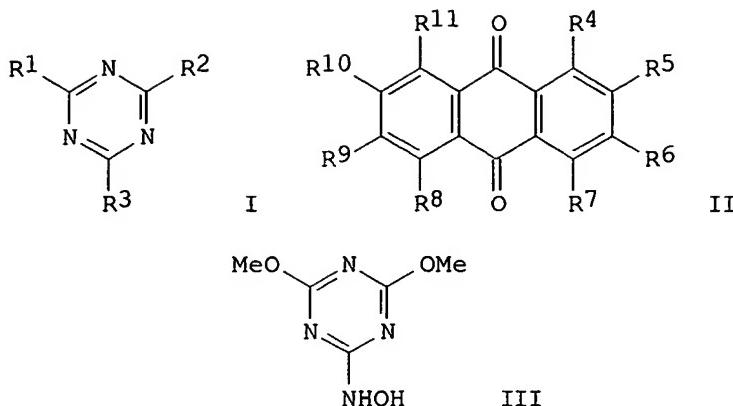
Methanimidamide, N-[1,3-bis(cyclopropylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]-N'-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



L23 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1991:666679 Document No. 115:266679 Processing of silver halide color photographic material. Abe, Akira; Ikegawa, Akihiko (Fuji Photo Film Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 03073948 A2 19910328 Heisei, 39 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1989-210833 19890816.

GI



AB In the processing of the title material, at least one of the processing solns. in the bleaching, washing, and stabilization processes contain a compd. selected from triazines I (R1-R3 = H, halogen, alkyl, amino, alkoxy, etc.), A(L)nB (B = a heterocyclic ring residue; L = a divalent linking group; n = 0 or 1), and quinones II (R4-R11 = H, halogen, alkyl, aryl, alkoxy, cyano, etc.). III is an example of I. The total amt. of replenishing solns. for the processing solns. is  $\leq 2500 \text{ mL/m}^2$  of the title material. The title processing method gives excellent images and saves replenishing solns.

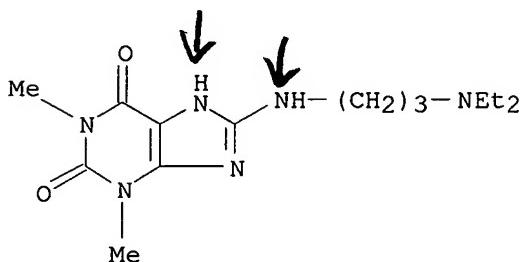
IT 137460-93-6

RL: USES (Uses)

(photog. processing soln. contg.)

RN 137460-93-6 HCPLUS

CN 1H-Purine-2,6-dione, 8-[3-(diethylamino)propyl]amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L23 ANSWER 9 OF 36 HCPLUS COPYRIGHT 2002 ACS

1991:631576 Document No. 115:231576 Auxochromic effect of substituents at the 8 position of 1,3,7-trimethylxanthine on the electronic spectra.  
Iovchev, I.; Zlatkov, A.; Peikov, P.; Gagauzov, I. (MA, Sofia, Bulg.). Farmatsiya (Sofia, Bulgaria), 41(2), 1-5 (Bulgarian) 1991. CODEN: FMTYA2. ISSN: 0428-0296.

AB Basic substituents in the 8 position of caffeine shifted the UV absorption band at 276 nm to 281-294 nm. Strongest effect was noted with N-bound substituents.

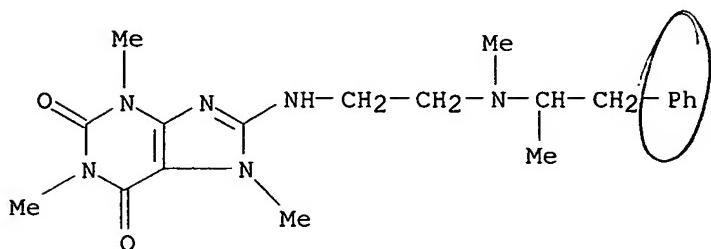
IT 28947-50-4 136611-58-0 136611-61-5

137018-92-9

RL: PRP (Properties)  
(UV spectrum of)

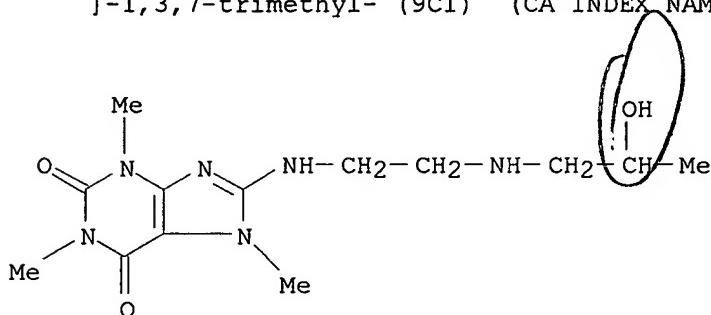
RN 28947-50-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(1-methyl-2-phenylethyl)amino]ethyl)amino]- (9CI) (CA INDEX NAME)



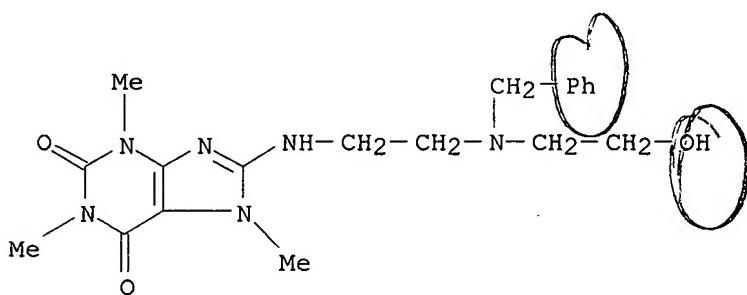
RN 136611-58-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[[2-[(2-hydroxypropyl)amino]ethyl]amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



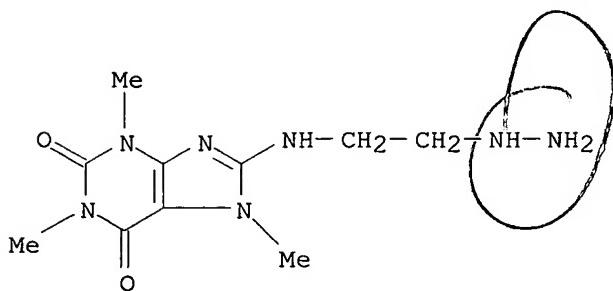
RN 136611-61-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[[2-[(2-hydroxyethyl)(phenylmethyl)amino]ethyl]amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

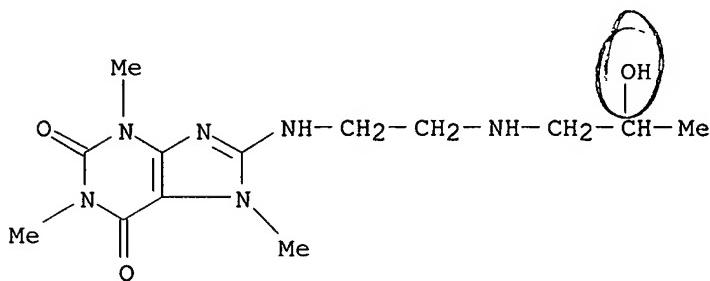


RN 137018-92-9 HCAPLUS

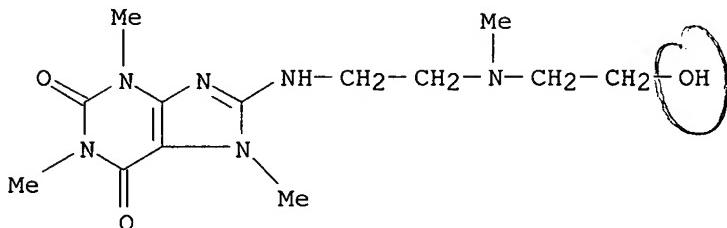
CN 1H-Purine-2,6-dione, 8-[(2-hydrazinoethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



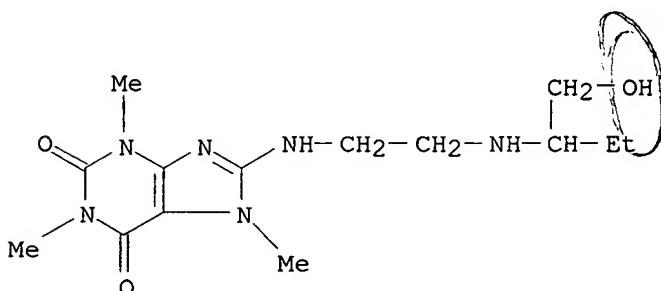
- L23 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2002 ACS  
 1991:582936 Document No. 115:182936 Synthesis of (2-aminoethyl)amino derivatives of caffeine. Zlatkov, A.; Peikov, P.; Gagauzov, I. (Nauchen Inst. Farmakol. Farm., MA, Sofia, Bulg.). Farmatsiya (Sofia, Bulgaria), 41(1), 1-4 (Bulgarian) 1991. CODEN: FMTYA2. ISSN: 0428-0296. OTHER SOURCES: CASREACT 115:182936.
- AB Aminolysis of 8-[(2-bromoethyl)amino]caffeine with 4 equiv RNHR1 [R = H, R1 = CH<sub>2</sub>CHMeOH, CHEtCH<sub>2</sub>OH, CH<sub>2</sub>CH<sub>2</sub>Ph, CHMeCH<sub>2</sub>Ph; R = Me, PhCH<sub>2</sub>, R1 = CH<sub>2</sub>CH<sub>2</sub>OH; RR1N = (CH<sub>2</sub>)<sub>6</sub>N, 3-(4-bromophenyl)morpholino] at 100.degree. for 3-180 min gave 55-75% title compds., identified by their IR and UV spectra.
- IT 136611-58-0P 136611-59-1P 136611-60-4P  
 136611-61-5P 136611-62-6P 136611-63-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)
- RN 136611-58-0 HCAPLUS
- CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(2-[(2-hydroxypropyl)amino]ethyl)amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



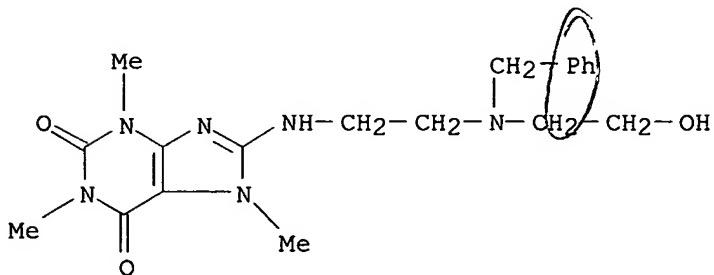
- RN 136611-59-1 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(2-[(2-hydroxyethyl)methylamino]ethyl)amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



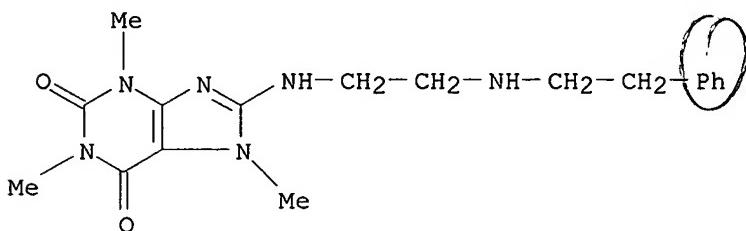
- RN 136611-60-4 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(2-[(1-hydroxymethyl)propyl]amino)ethyl]amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 136611-61-5 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[[2-[(2-hydroxyethyl)(phenylmethyl)amino]ethyl]amino]-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

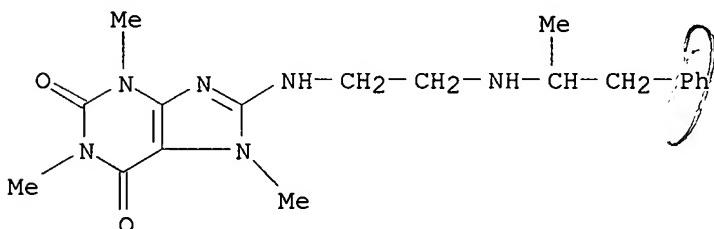


RN 136611-62-6 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[[2-[(2-phenylethyl)amino]ethyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



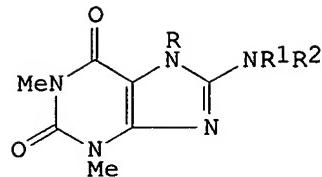
● HCl

RN 136611-63-7 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[[2-[(1-methyl-2-phenylethyl)amino]ethyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L23 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2002 ACS  
1990:604407 Document No. 113:204407 Synthesis and preliminary pharmacological screening of some 8-substituted methylxanthines.  
Drabczynska, Anna; Pawlowski, Maciej; Gorczyca, Maria; Malec, Danuta;  
Modzelewski, Jerzy (Dep. Pharm. Chem., Med. Acad., Krakow, 31-065, Pol.).  
Polish Journal of Pharmacology and Pharmacy, 41(4), 385-94 (English) 1989.



AB Methods of synthesis, chem. properties and results of preliminary pharmacol. screening for 8-amino substituted caffeine derivs. [I, R = Me, NR1R2 = NH<sub>2</sub>, NHCH<sub>2</sub>Ph, or N(CH<sub>2</sub>Ph)<sub>2</sub>] and of 8-aminotheophylline 7,8-disubstituted derivs. (I, R = CH<sub>2</sub>Ph, R<sub>1</sub> = H, R<sub>2</sub> = (CH<sub>2</sub>)<sub>n</sub>X; X = NHBu or NBu<sub>2</sub> and n = 2 or 3) are described. The compds. show weak sedative and antidepressive activity and some of them also small antinociceptive effect.

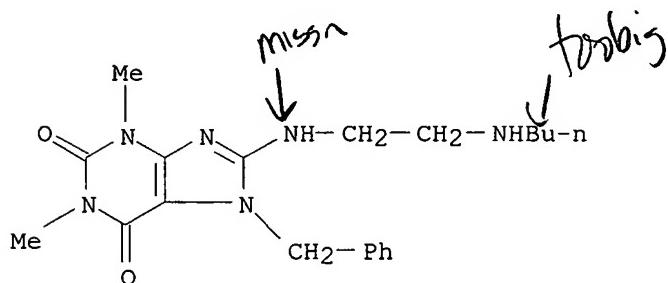
IT 130187-59-6P 130187-60-9P 130187-61-0P

130187-62-1P 130187-63-2P 130187-64-3P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (prep. and pharmacol. of)

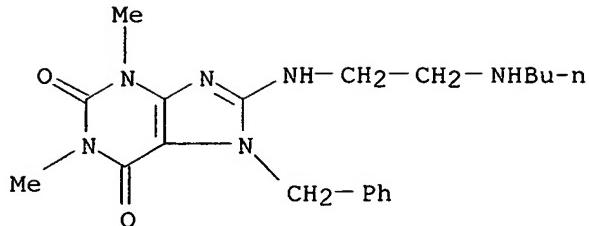
RN 130187-59-6 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(2-(butylamino)ethyl]amino]-3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 130187-60-9 HCPLUS

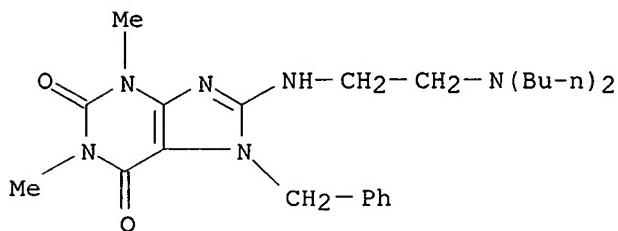
CN 1H-Purine-2,6-dione, 8-[(2-(butylamino)ethyl]amino]-3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 130187-61-0 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-(dibutylamino)ethyl)amino]-3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)- (9CI) (CA INDEX NAME)



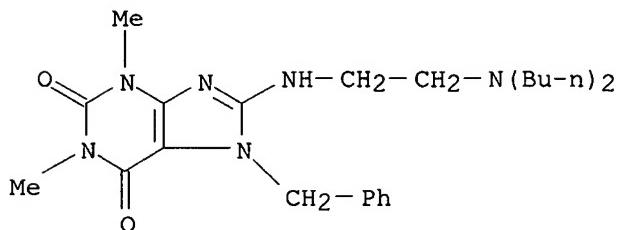
RN 130187-62-1 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-(dibutylamino)ethyl)amino]-3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 130187-61-0

CMF C24 H36 N6 O2

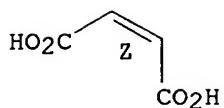


CM 2

CRN 110-16-7

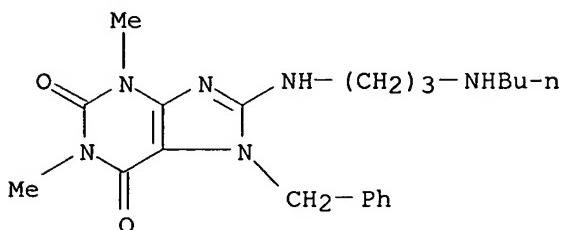
CMF C4 H4 O4

Double bond geometry as shown.



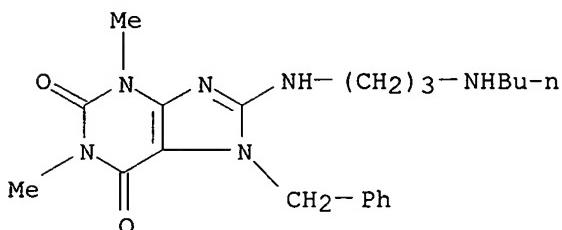
RN 130187-63-2 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[[3-(butylamino)propyl]amino]-3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 130187-64-3 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[[3-(butylamino)propyl]amino]-3,7-dihydro-1,3-dimethyl-7-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L23 ANSWER 12 OF 36 HCAPIUS COPYRIGHT 2002 ACS

1990:213569 Document No. 112:213569 Tridentate conjugates for competitive immunoassays. Oh, Chan S.; Sternberg, James C. (Beckman Instruments, Inc., USA). Eur. Pat. Appl. EP 310361 A2 19890405, 40 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1988-309002 19880929. PRIORITY: US 1987-103093 19870930.

AB A tridentate conjugate for competitive immunoassays has 3 chem. moieties, or tridentate members, attached through an appropriate spacer moiety. At least 2 of the tridentate members are relatively small mols. (e.g. ligands, haptens), usually < 7000 daltons. The particular appropriate spacer moiety selected for a tridentate imparts certain steric properties to the tridentate conjugate. In 1 embodiment, the binding of a macromol. specific binding partner to one of the tridentate members sterically inhibits the binding of a different macromol. to another tridentate member. In another embodiment, the binding of a 1st tridentate member to a macromol. restricts the subsequent binding of a 2nd tridentate member to a proximate location on the same macromol. Thus, a

biotin-theophylline-lysine conjugate (prepn. described) was reacted with DNP-bis(aminocaproic acid) N-hydroxysuccinimide ester (prepn. described) to form a biotin-theophylline-DNP conjugate. Theophylline amine (I) was detd. in a nephelometric inhibition immunoassay by mixing the conjugate with anti-theophylline monoclonal antibody, anti-DNP antibody, avidin, and samples contg. the analyte. Free I competed with theophylline in the conjugate for the anti-theophylline monoclonal antibody. Increasing concns. of I resulted in an increased nephelometric signal.

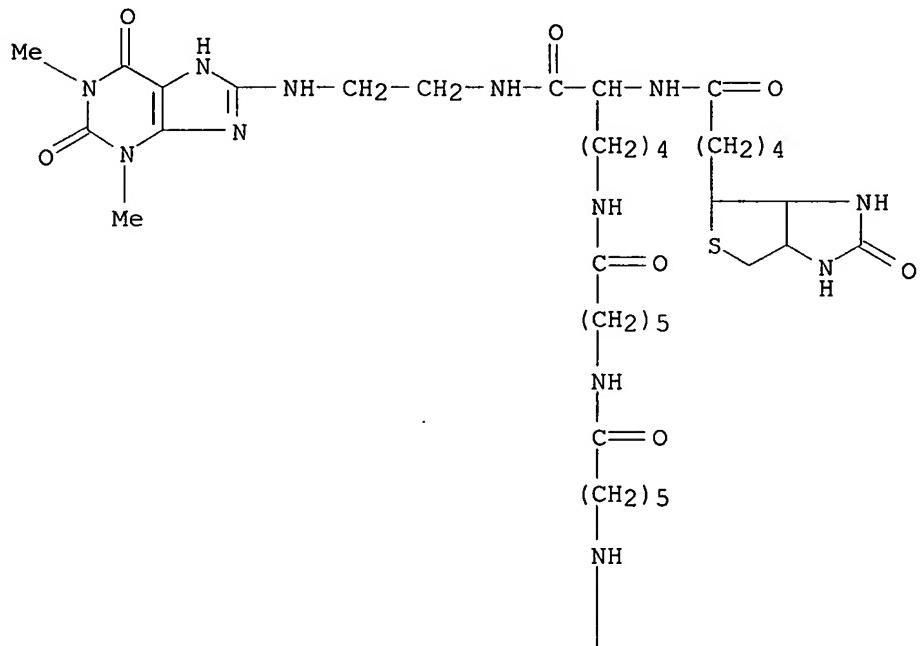
IT 127067-75-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, for competitive immunoassays)

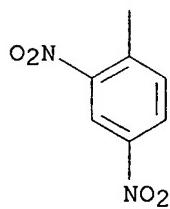
RN 127067-75-8 HCPLUS

CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[5-[[6-[[6-[(2,4-dinitrophenyl)amino]-1-oxohexyl]amino]-1-oxohexyl]amino]-1-[[[2-[(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)amino]ethyl]amino]carbonyl]pentyl]hexahydro-2-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



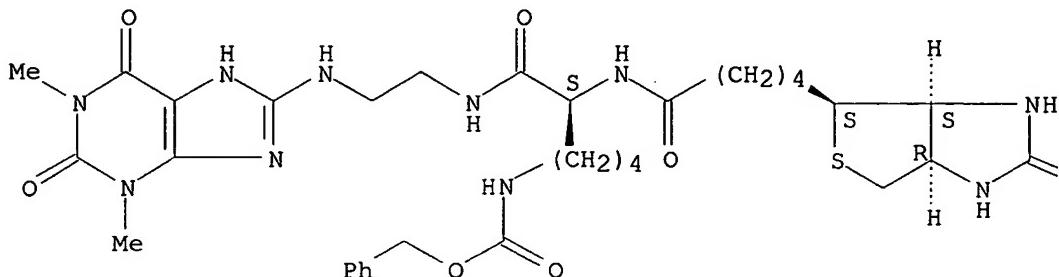
IT 126379-67-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, in conjugate prepn. for competitive immunoassay)

RN 126379-67-7 HCPLUS  
CN Carbamic acid, [5-[{5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl}amino]-6-oxo-6-[[2-[(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)amino]ethyl]amino]hexyl]-, phenylmethyl ester,  
[3aS-[3a.alpha.,4.beta.-(R\*),6a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

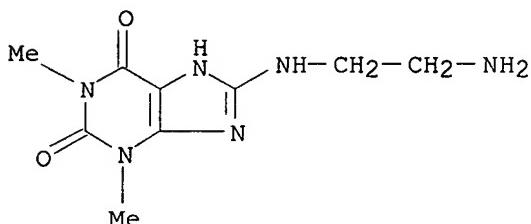
PAGE 1-A



PAGE 1-B

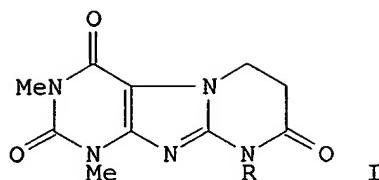
$\equiv_O$

IT 14251-32-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with biotinylcarbobenzoxylysine)  
RN 14251-32-2 HCPLUS  
CN 1H-Purine-2,6-dione, 8-[(2-aminoethyl)amino]-3,7-dihydro-1,3-dimethyl-  
(9CI) (CA INDEX NAME)



L23 ANSWER 13 OF '36 HCAPLUS COPYRIGHT 2002 ACS  
1989:553744 Document No. 111:153744 Synthesis of some 9-(aminoalkyl)-6,7-dihydropyrimido[2,1-f]purine-2,4,8(1H,3H,9H)-triones. Pawłowski, Maciej; Buschauer, Armin; Schunack, Walter (Dep. Pharm. Chem., N. Copernicus Med. Acad., Krakow, 31-065, Pol.). Archiv der Pharmazie (Weinheim, Germany), 322(7), 447-9 (English) 1989. CODEN: ARPMAS. ISSN: 0365-6233. OTHER SOURCES: CASREACT 111:153744.

GI



AB The title compds. I [R = (CH<sub>2</sub>)<sub>m</sub>NH<sub>2</sub>, (CH<sub>2</sub>)<sub>n</sub>Ac<sub>2</sub>; n = 2,3] were prep'd. by alkylation of dihydropyrimido[2,1-f]purinetrione I (R = H) with N-(bromoalkyl)phthalimides, followed by hydrazinolysis and recyclization of the dihydropyrimidinone ring.

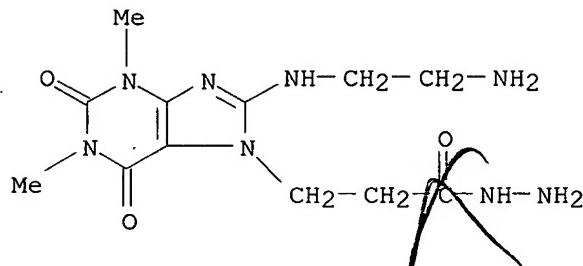
IT 122606-42-2P 122606-43-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prep'n. and acidic hydrolysis of, carboxylic acid from)

RN 122606-42-2 HCPLUS

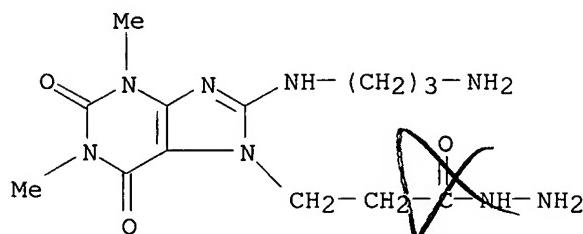
CN 7H-Purine-7-propanoic acid, 8-[(2-aminoethyl)amino]-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-, hydrazide, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 122606-43-3 HCPLUS

CN 7H-Purine-7-propanoic acid, 8-[(3-aminopropyl)amino]-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-, hydrazide, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

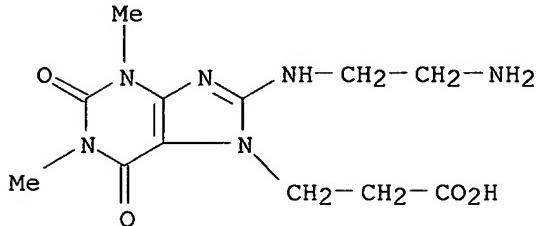
IT 122606-44-4P 122606-47-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)  
 (prepn. and cyclization of)

RN 122606-44-4 HCPLUS

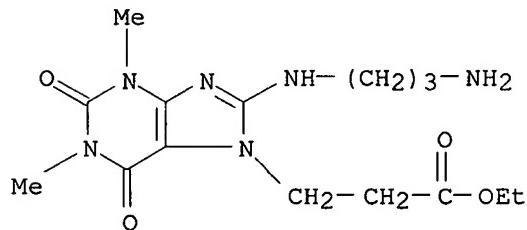
CN 7H-Purine-7-propanoic acid, 8-[(2-aminoethyl)amino]-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 122606-47-7 HCPLUS

CN 7H-Purine-7-propanoic acid, 8-[(3-aminopropyl)amino]-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-, ethyl ester, dihydrochloride (9CI) (CA INDEX NAME)

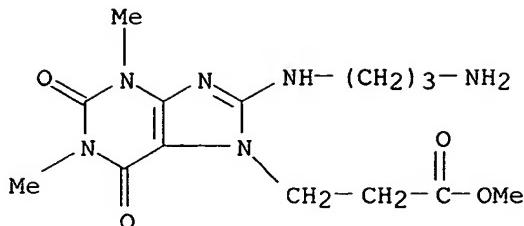


● 2 HCl

IT 122606-46-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

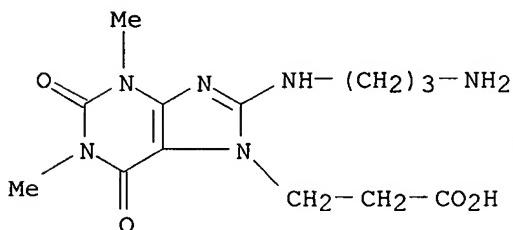
RN 122606-46-6 HCPLUS

CN 7H-Purine-7-propanoic acid, 8-[(3-aminopropyl)amino]-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-, methyl ester, dihydrochloride (9CI) (CA INDEX NAME)



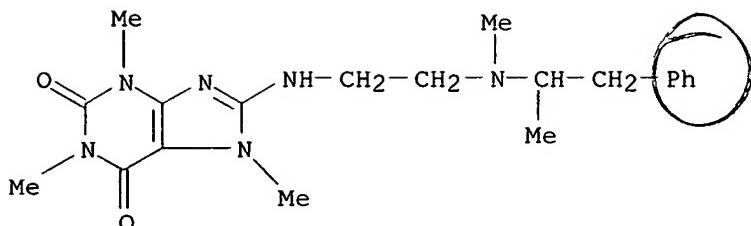
● 2 HCl

IT 122606-45-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prep., cyclization, and esterification of)  
 RN 122606-45-5 HCPLUS  
 CN 7H-Purine-7-propanoic acid, 8-[(3-aminopropyl)amino]-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L23 ANSWER 14 OF 36 HCPLUS COPYRIGHT 2002 ACS  
 1982:116995 Document No. 96:116995 Circular paper chromatography for the toxicological detection of drugs. Moraes, Ester de Camargo Fonseca; Sznelwar, Rywka Bandklajder (Fac. Cienc. Farm., Univ. Sao Paulo, Sao Paulo, Brazil). Revista de Farmacia e Bioquimica da Universidade de Sao Paulo, 17(2), 218-33 (Portuguese) 1981. CODEN: RFBUBI. ISSN: 0370-4726.  
 AB Fifty-two drugs were detd. by circular paper chromatog. using 15 different chromogenic reagents of which 10 were deemed more suitable for this type of detn. due to the greater sensitivity and specificity of their reactions. The prep. of each of the chromogenic reagents is described. The importance of rapid, simple, and reliable methods in the forensic detection of drugs is discussed.  
 IT 28947-50-4  
 RL: ANT (Analyte); ANST (Analytical study)  
 (detection of, by circular paper chromatog.)  
 RN 28947-50-4 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[[2-[methyl(1-methyl-2-phenylethyl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)



L23 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1979:180469 Document No. 90:180469 Evidence for the cell surface locus of presynaptic purine nucleotide receptors in the guinea pig ileum.

Okwuasaba, F. K.; Hamilton, J. T.; Cook, M. A. (Dep. Pharmacol., Univ. Western Ontario, London, Ont., Can.). *J. Pharmacol. Exp. Ther.*, 207(3), 779-86 (English) 1978. CODEN: JPETAB. ISSN: 0022-3565.

**AB** Elec. stimulated longitudinal muscle strip of the guinea pig ileum was used to study the locus of action of adenosine [58-61-7] and theophylline [58-55-9] which were covalently coupled to an oxidized oligosaccharide to produce large mol. wt. compds. which were confined to the extracellular space. Adenosine and related compds., as well as the adenosine deriv., stachyose-iminobis(porpyl amino)purine rebose (STADO) [69227-86-7] produced concn.-dependent inhibition of twitch response of guinea pig ileum at low frequencies (0.2-1.0 Hz) of stimulation. The inhibitory effect of STADO was slower in onset and more prolonged in duration than those to adenosine and related compds. Theophylline and the deriv. stachyose-aminoethylaminotheophylline (STATHE) at low concn. (25-75 .mu.M) selective antagonized the effects of adenosine and related compds. as well as STADO, while not affecting the response to noradrenaline bitartrate [51-40-1]. Schild plots yielded apparent pA<sub>2</sub> values for theophylline of 4.7, 4.68 and 4.66 and for STATHE of 4.57, 4.59, and 4.56 for ATP [56-65-5], adenosine, and STADO, resp., and possessed slopes which were not significantly different from 1. Dipyridamole (9.9 .times. 10<sup>-7</sup>M) decreased the twitch response to elec. stimulation without affecting the response to exogenous acetylcholine. In addn., Dipyridamole significantly augmented the response to ATP, adenosine, and 6-methylaminopurine riboside [1867-73-8], producing 48.12-, 47.62-, and 40.81-fold decreased resp. in their EC<sub>50</sub> values. In contrast, Dipyridamole did not alter the EC<sub>50</sub> values of noradrenaline and STADO (decreases were 0.98- and 1.24-fold, resp.). The results are discussed in relation to the cell surface localization of presynaptic purinergic receptors in the guinea pig ileum.

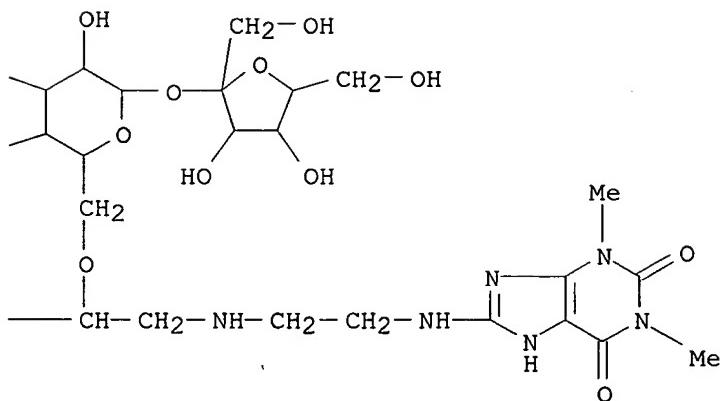
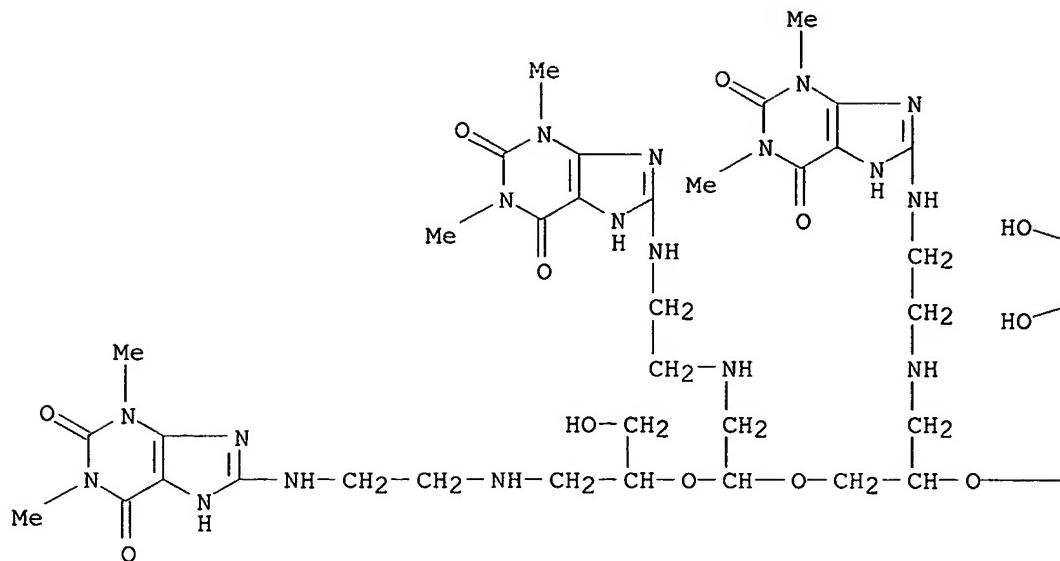
**IT** 69227-87-8

RL: BIOL (Biological study)

(intestine contraction response to, after adenosine inhibition)

RN 69227-87-8 HCAPLUS

CN .alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl 6-O-[8-(hydroxymethyl)-12-[(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)amino]-1,3,6-tris[[[2-[(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)amino]ethyl]amino]methyl]-2,5,7-trioxa-10-azadodec-1-yl]-, [1S-(1R\*,3R\*,6R\*,8S\*)]- (9CI) (CA INDEX NAME)



L23 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1975:38389 Document No. 82:38389 Determination of dl-fencamine in rat and human urine. Mallol, J.; Pitarch, L.; Coronas, R.; Pons, A., Jr. (Inst. Miquel Invest. Ter., S.A., Barcelona, Spain). Arzneim.-Forsch., 24(9), 1301-4 (English) 1974. CODEN: ARZNAD.

GI For diagram(s), see printed CA Issue.

AB Twenty-four hr after oral administration of dl-fencamine (I) [33303-21-8] to female and male rats, 14.2 and 9.26%, resp., of I were eliminated in urine; most of I was excreted in the first 3 hr. After

48 hr no I was detected in the urine. No differences were obsd. in elimination in rats treated orally or i.v. In man, 26.6% of I was excreted in the first 24 hr.

IT 33303-21-8  
RL: ANT (Analyte); ANST (Analytical study)  
(detn. of, in urine)  
RN. 33303-21-8 HCAPLUS

L23 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1973:492274 Document No. 79:92274 Trisubstituted ethylenediamine derivatives. (Laboratorios Miquel S. A.). Span. ES 385302 19730416, 14 pp. (Spanish). CODEN: SPXXAD. APPLICATION: ES 1970-385302 19701022.

GI For diagram(s), see printed CA Issue.

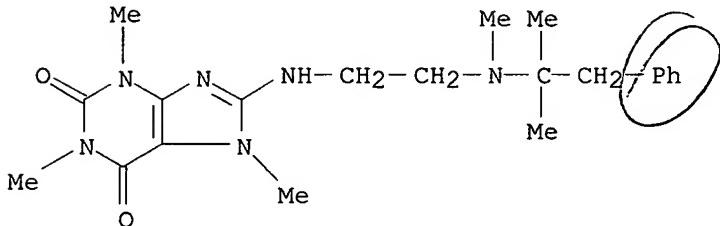
AB Caffeine derivs. I (R = Me, Et, Pr, CHMe<sub>2</sub>, Bu, CH<sub>2</sub>CHMe<sub>2</sub>, cyclohexyl, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, 2-pyridyl, allyl; R<sub>1</sub> = 3,4-(MeO)2C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>CHMe, PhCH<sub>2</sub>CHMe, PhCH(OH)CHMe, PhCH<sub>2</sub>CMe<sub>2</sub>, 3-HOC<sub>6</sub>H<sub>4</sub>CH(OH)CH<sub>2</sub>, PhCH<sub>2</sub>, PhCHMe, cyclohexyl, 2,2,3-trimethylbicyclo[2.2.1]hept-3-yl, Et, Pr, Bu, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, 3-pyridylmethyl; NRR<sub>1</sub> = morpholino, piperidino) were prep'd. by treating 8-chlorocaffeine with H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NRR<sub>1</sub>. I are central nervous system stimulants.

IT 33236-47-4P 33236-49-6P 33236-52-1P  
33236-53-2P 33236-54-3P 33236-55-4P  
33236-56-5P 33236-57-6P 33236-58-7P  
33303-21-8P 33303-22-9P 33403-58-6P  
33403-59-7P 50279-90-8P 50298-66-3P  
50298-67-4P 50298-68-5P 50298-69-6P  
50298-70-9P 50298-71-0P 50298-72-1P  
50298-73-2P 50331-86-7P 50331-90-3P  
50416-34-7P 50940-07-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of)

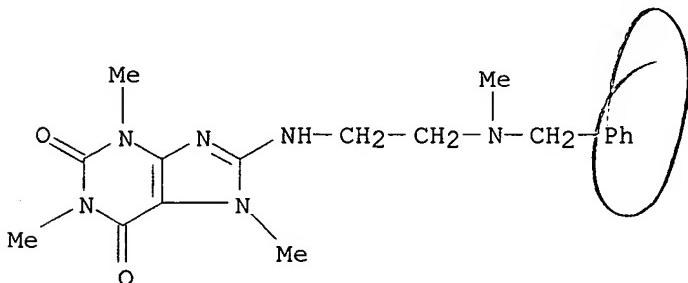
RN 33236-47-4 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[[2-[(1,1-dimethyl-2-phenylethyl)methylamino]ethyl]amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



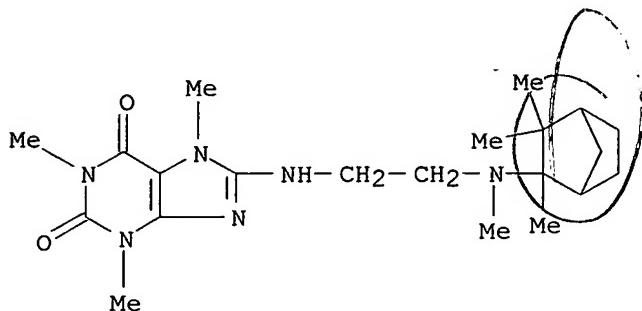
RN 33236-49-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[[2-[methyl(phenylmethyl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)



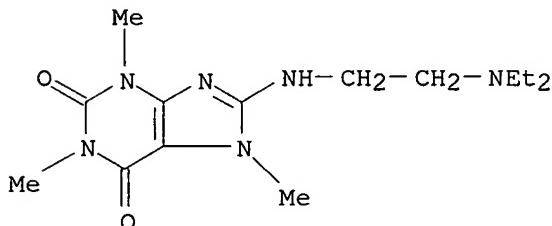
RN 33236-52-1 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(2,3,3-trimethylbicyclo[2.2.1]hept-2-yl)amino]ethyl)amino]- (9CI) (CA INDEX NAME)



RN 33236-53-2 HCAPLUS

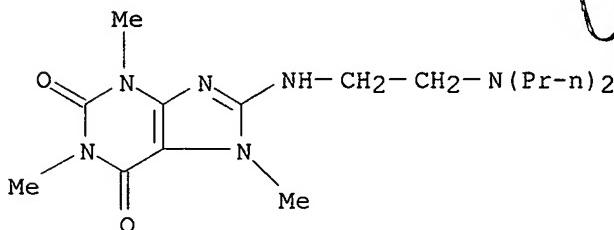
CN 1H-Purine-2,6-dione, 8-[(2-(diethylamino)ethyl)amino]-3,7-dihydro-1,3,7-trimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

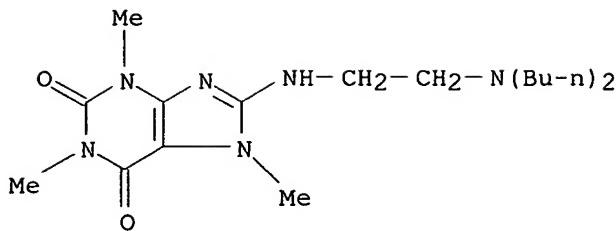
RN 33236-54-3 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-(dipropylamino)ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

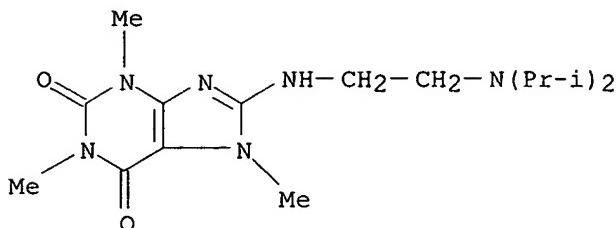


RN 33236-55-4 HCAPLUS

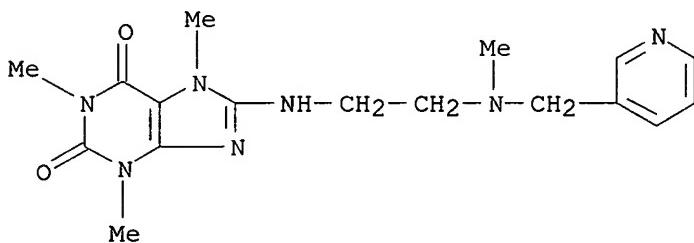
CN 1H-Purine-2,6-dione, 8-[(2-(dibutylamino)ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



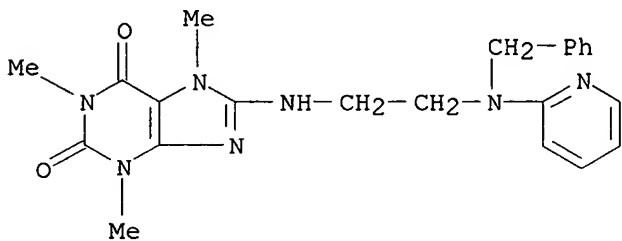
RN 33236-56-5 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[(2-[bis(1-methylethyl)amino]ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 33236-57-6 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(3-pyridinylmethyl)amino]ethyl)amino]- (9CI) (CA INDEX NAME)

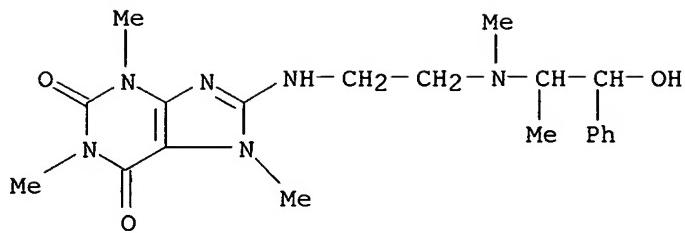


RN 33236-58-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[(phenylmethyl)-2-pyridinylamino]ethyl)amino]- (9CI) (CA INDEX NAME)



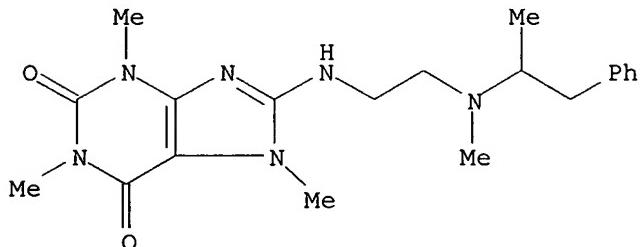
RN 33303-21-8 HCAPLUS  
RN 33303-22-9 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(2-[(2-hydroxy-1-methyl-2-phenylethyl)methylamino]ethyl)amino]-1,3,7-trimethyl-, hydrochloride (9CI)

(CA INDEX NAME)



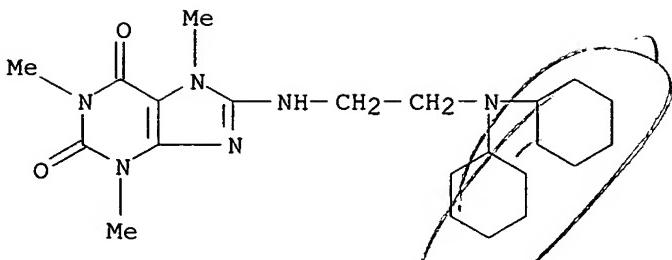
●x HCl

RN 33403-58-6 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(1-methyl-2-phenylethyl)amino]ethyl)amino]-, hydrochloride (9CI) (CA INDEX NAME)

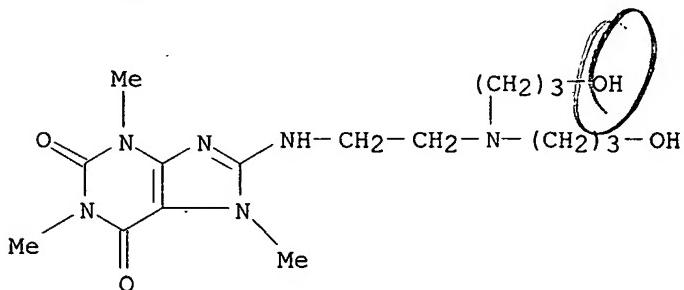


●x HCl

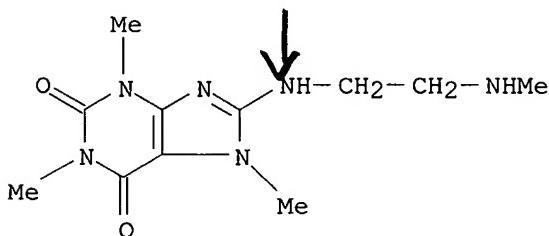
RN 33403-59-7 HCPLUS  
RN 50279-90-8 HCPLUS  
RN 50298-66-3 HCPLUS  
RN 50298-67-4 HCPLUS  
RN 50298-68-5 HCPLUS  
RN 50298-69-6 HCPLUS  
RN 50298-70-9 HCPLUS  
RN 50298-71-0 HCPLUS  
RN 50298-72-1 HCPLUS  
RN 50298-73-2 HCPLUS  
RN 50331-86-7 HCPLUS  
CN 1H-Purine-2,6-dione, 8-[(2-(dicyclohexylamino)ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 50331-90-3 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(2-[bis(3-hydroxypropyl)amino]ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 50416-34-7 HCAPLUS  
 RN 50940-07-3 HCAPLUS  
 IT 33584-84-8  
 RL: RCT (Reactant)  
 (reaction of, with phenylisopropyl bromide)  
 RN 33584-84-8 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-methylamino)ethyl]amino- (9CI) (CA INDEX NAME)



*ES 385302*

L23 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2002 ACS  
 1973:474437 Document No. 79:74437 Chromatographic screening for drugs of abuse using capillary columns. I. Comparison of open tubular columns and support coated open tubular columns for the analysis of central nervous system stimulant drugs. Caddy, B.; Fish, F.; Scott, D. (Sch. Pharm. Sci., Univ. Strathclyde, Glasgow, Scot.). Chromatographia, 6(6), 251-6 (English) 1973. CODEN: CHRGB7.  
 AB Thirty-three central nervous system stimulant drugs, esp. amphetamines, in ethereal urine exts. were sep'd. and detd. (limiting) by routine capillary-liq. chromotog. on 10 m support-coated, open tubular glass columns. Unsatisfactory sepn. was achieved with steel or glass open tubular columns silanized or treated with surface active agents, such as Na lauryl phosphate or Tween 80, and with direct injection of urine

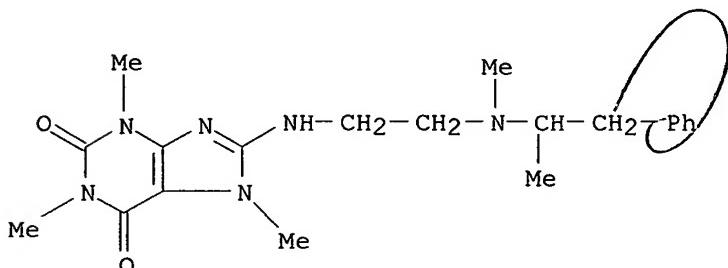
samples. Support-coated, open tubular columns combined the advantages of both open tubular and packed columns through larger sample vol., increased adsorption surface, decreased bleed off, and elimination of the stream splitter.

IT 28947-50-4

RL: ANT (Analyte); ANST (Analytical study)  
(chromatog. of)

RN 28947-50-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(1-methyl-2-phenylethyl)amino]ethyl)amino]- (9CI) (CA INDEX NAME)



L23 ANSWER 19 OF 36 HCPLUS COPYRIGHT 2002 ACS

1973:72181 Document No. 78:72181 8-Aminothephylline derivatives.

(Laboratoire Lebrun S. A.). Fr. Demande FR 2116302 19720818, 15 pp.  
(French). CODEN: FRXXBL. APPLICATION: FR 1970-43891 19701207.

GI For diagram(s), see printed CA Issue.

AB 8-Aminothephyllines I (R = alkyl, aralkyl, hydroxyalkyl, chloroalkyl, aminoalkyl; R<sub>1</sub> = alkyl, aralkyl, aminoalkyl; NRR<sub>1</sub> = substituted piperazino, piperidino, pyrrolidino) (52 compds.) were prepd. by treating 8-chlorothephylline or 8-bromotheophylline with RR<sub>1</sub>NH. I displayed coronary dilator, diuretic, spasmolytic, and bronchodilator activities greater than that of theophylline, accompanied by lower toxicity.

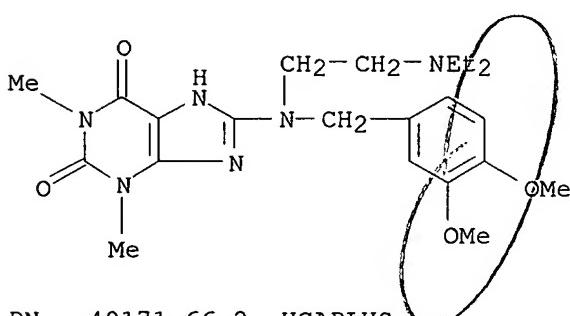
IT 40171-52-6P 40171-66-2P 40171-67-3P

40171-68-4P 40171-69-5P 40171-80-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

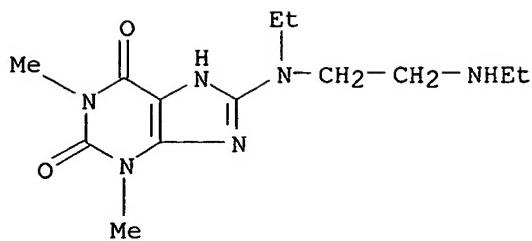
RN 40171-52-6 HCPLUS

CN 1H-Purine-2,6-dione, 8-[[2-(diethylamino)ethyl][(3,4-dimethoxyphenyl)methyl]amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



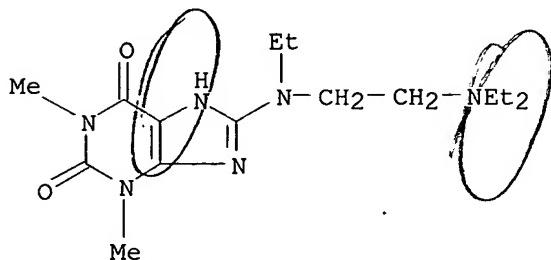
RN 40171-66-2 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(ethyl[2-(ethylamino)ethyl]amino)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



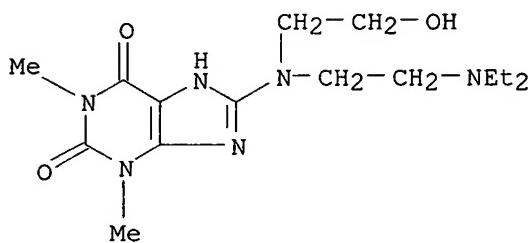
RN 40171-67-3 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-(diethylamino)ethyl)ethylamino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 40171-68-4 HCAPLUS

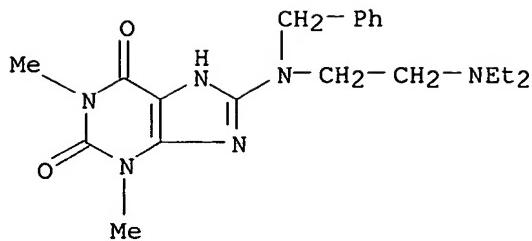
CN 1H-Purine-2,6-dione, 8-[(2-(diethylamino)ethyl)(2-hydroxyethyl)amino]-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 40171-69-5 HCAPLUS

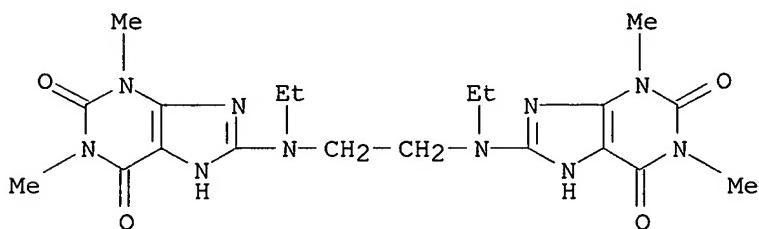
CN 1H-Purine-2,6-dione, 8-[(2-(diethylamino)ethyl)(phenylmethyl)amino]-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 40171-80-0 HCPLUS

CN 1H-Purine-2,6-dione, 8,8'-(1,2-ethanediylbis(ethylimino))bis[3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L23 ANSWER 20 OF 36 HCPLUS COPYRIGHT 2002 ACS

1971:518345 Document No. 75:118345 Reaction of 8-[2-(methylamino)ethylamino]caffeine with 2-bromopropylbenzene. (Instituto de Investigaciones Terapeuticas, S. A.). Span. ES 367815 19710416, 5 pp. Addn. to Span. 347,509. (Spanish). CODEN: SPXXAD. APPLICATION: ES 19690519.

GI For diagram(s), see printed CA Issue.

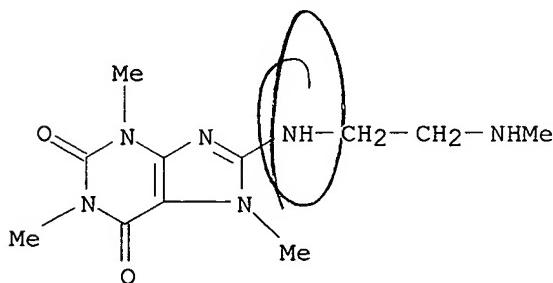
AB 8-[2-(Methylamino)ethylamino]caffeine (I) (1:1 ratio) is refluxed 8 hr in EtOH with PhCH<sub>2</sub>CHBrMe and Na<sub>2</sub>CO<sub>3</sub> to give an analeptic, psychotonic, antidepressive, and antispasmodic compd., m. 153-5.degree..

IT 33584-84-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 33584-84-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[2-(methylamino)ethyl]amino- (9CI) (CA INDEX NAME)



L23 ANSWER 21 OF 36 HCPLUS COPYRIGHT 2002 ACS  
1971:420447 Document No. 75:20447 Pharmacologically-active ethylenediamine derivatives. Miquel Quintilla, Juan (Instituto de Investigaciones Terapeuticas, S. A.). S. African ZA 6907921 19700825, 7 pp. (English).  
CODEN: SFXXAB. PRIORITY: ES 19690519.

GI For diagram(s), see printed CA Issue.

AB The caffeine deriv. (I) showed analeptic, psychotonic, antidepressive, and antispasmodic properties. Rats treated with I showed improved appetite but no. increase in wt. compared with undosed controls. I.p. LD<sub>50</sub> was 93.4 mg/kg and oral LD<sub>50</sub> 512 mg/kg. Refluxing a mixt. of 0.25 mole N-methyl-N-(8-caffeinyl)ethylenediamine, 0.25 mole PhCH<sub>2</sub>CHBrMe, 0.14 mole Na<sub>2</sub>CO<sub>3</sub> and 700 EtOH 8 hr gave I, m. 153-5.degree.. I was also prep'd. from 8-chlorocaffeine and PhCH<sub>2</sub>CHMeCHNMeCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, b10 125-30.degree.. I formed a hydrochloride, m. 280-3.degree. and a picrate, m. 277.degree..

IT 28947-40-2P 28947-50-4P 33246-03-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

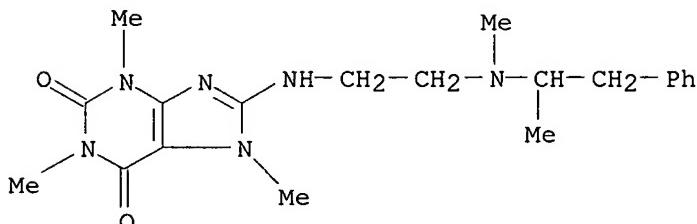
RN 28947-40-2 HCPLUS

CN Caffeine, 8-[(2-[methyl(.alpha.-methylphenethyl)amino]ethyl)amino]-, picrate (8CI) (CA INDEX NAME)

CM 1

CRN 28947-50-4

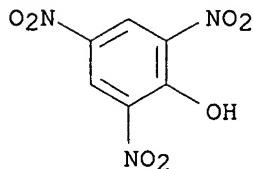
CMF C20 H28 N6 O2



CM 2

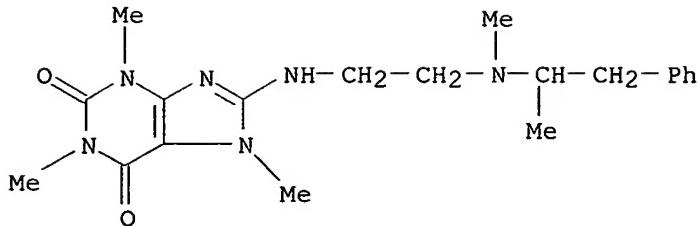
CRN 88-89-1

CMF C6 H3 N3 O7



RN 28947-50-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(1-methyl-2-phenylethyl)amino]ethyl)amino]- (9CI) (CA INDEX NAME)



RN 33246-03-6 HCAPLUS

L23 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1971:420324 Document No. 75:20324 Trisubstituted ethylenediamines. 1. Synthesis of trisubstituted ethylenediamines. Pitarch, L.; Iglesias, F.; Coronas, R. (Inst. Miquel Invest. Ter., Spain). Quim. Ind. (Madrid), 17(1), 71-6 (Spanish) 1971. CODEN: QUIBAL.

GI For diagram(s), see printed CA Issue.

AB I were prep'd. by reaction of 8-chlorocaffeine with amines or diamines. I has stimulant properties.

IT 33236-38-3P 33236-39-4P 33236-40-7P

33236-41-8P 33236-42-9P 33236-43-0P

33236-44-1P 33236-45-2P 33236-46-3P

33236-47-4P 33236-48-5P 33236-49-6P

33236-50-9P 33236-51-0P 33236-52-1P

33236-53-2P 33236-54-3P 33236-55-4P

33236-56-5P 33236-57-6P 33236-58-7P

33303-21-8P 33303-22-9P 33403-58-6P

33403-59-7P 33403-60-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of)

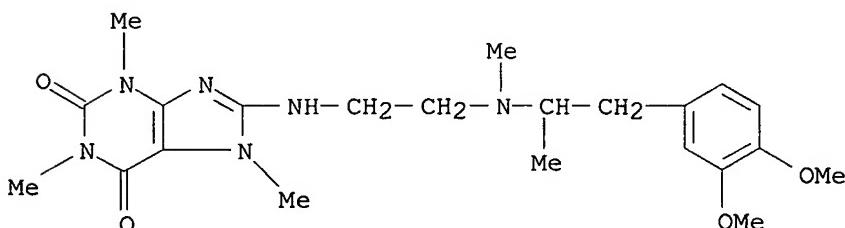
RN 33236-38-3 HCAPLUS

CN Caffeine, 8-[(2-[(3,4-dimethoxy-.alpha.-methylphenethyl)methylamino]ethyl]amino]-, picrate (8CI) (CA INDEX NAME)

CM 1

CRN 47707-55-1

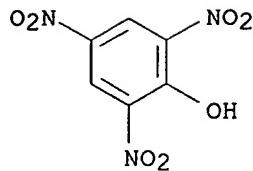
CMF C22 H32 N6 O4



CM 2

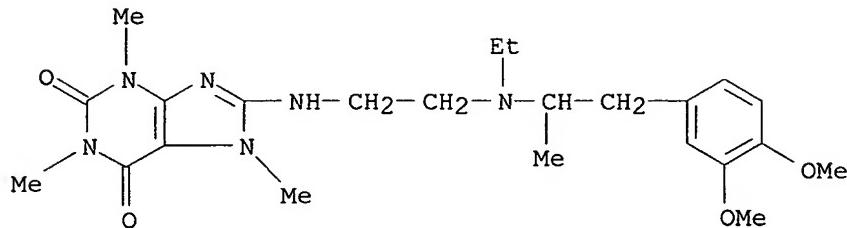
CRN 88-89-1

CMF C6 H3 N3 O7



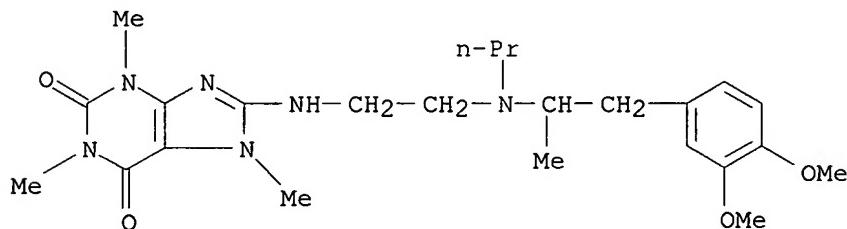
RN 33236-39-4 HCAPLUS

CN Caffeine, 8-[(2-[(3,4-dimethoxy-.alpha.-methylphenethyl)ethylamino]ethyl)amino]- (8CI) (CA INDEX NAME)



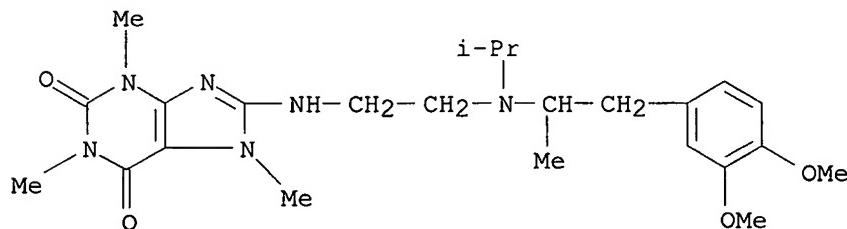
RN 33236-40-7 HCAPLUS

CN Caffeine, 8-[(2-[(3,4-dimethoxy-.alpha.-methylphenethyl)propylamino]ethyl)amino]- (8CI) (CA INDEX NAME)



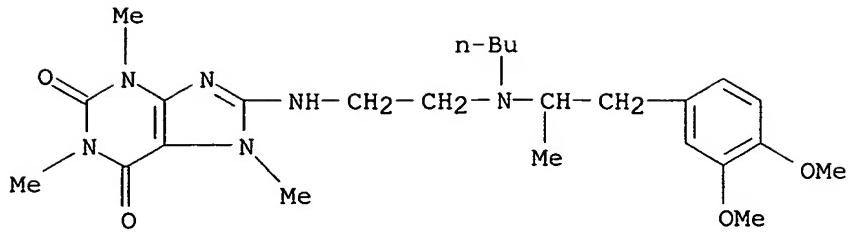
RN 33236-41-8 HCAPLUS

CN Caffeine, 8-[(2-[(3,4-dimethoxy-.alpha.-methylphenethyl)isopropylamino]ethyl)amino]- (8CI) (CA INDEX NAME)

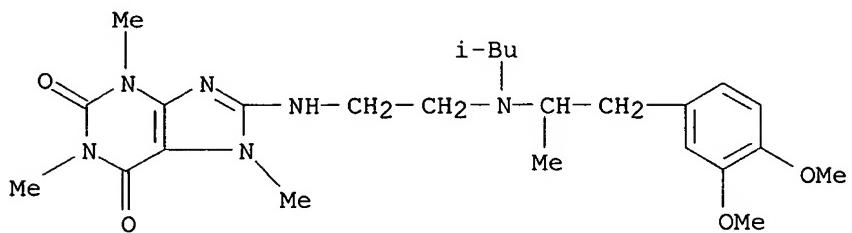


RN 33236-42-9 HCAPLUS

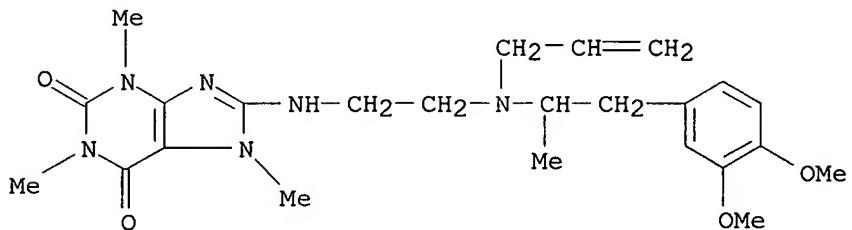
CN Caffeine, 8-[(2-[butyl(3,4-dimethoxy-.alpha.-methylphenethyl)amino]ethyl)amino]- (8CI) (CA INDEX NAME)



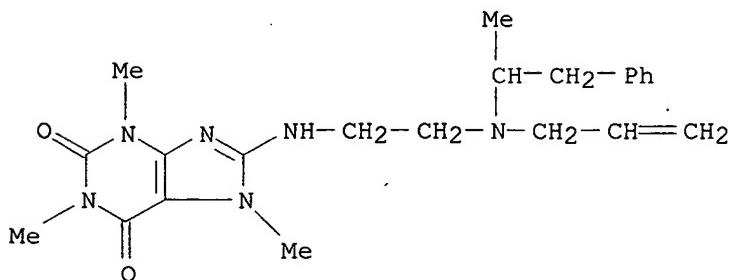
RN 33236-43-0 HCAPLUS  
CN Caffeine, 8-[2-[(3,4-dimethoxy-.alpha.-methylphenethyl)isobutylamino]ethyl]amino]- (8CI) (CA INDEX NAME)



RN 33236-44-1 HCAPLUS  
CN Caffeine, 8-[2-[(allyl(3,4-dimethoxy-.alpha.-methylphenethyl)amino)ethyl]amino]- (8CI) (CA INDEX NAME)

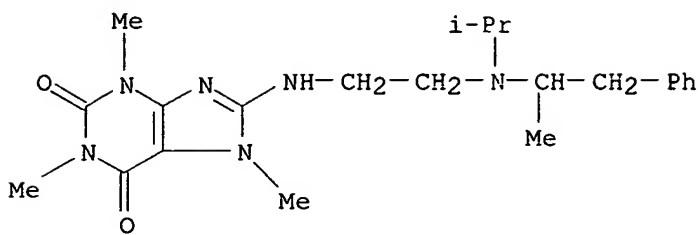


RN 33236-45-2 HCAPLUS  
CN Caffeine, 8-[2-[(allyl(.alpha.-methylphenethyl)amino)ethyl]amino]- (8CI) (CA INDEX NAME)



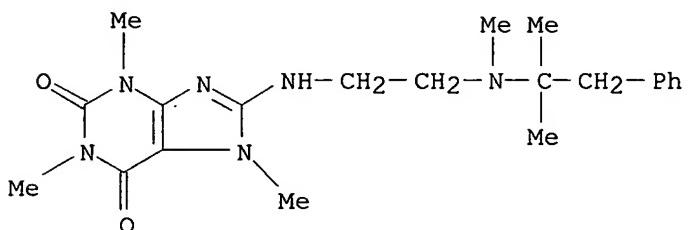
RN 33236-46-3 HCAPLUS  
CN Caffeine, 8-[2-[(isopropyl(.alpha.-methylphenethyl)amino)ethyl]amino]-

(8CI) (CA INDEX NAME)



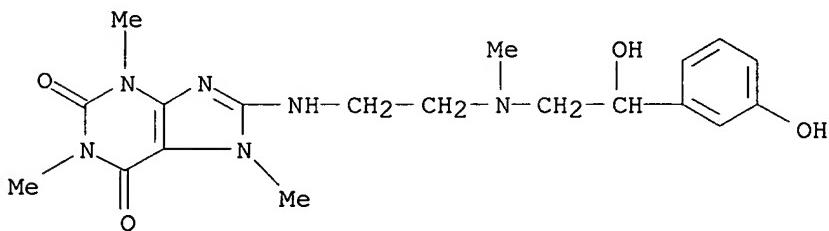
RN 33236-47-4 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[{2-[(1,1-dimethyl-2-phenylethyl)methylamino]ethyl}amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



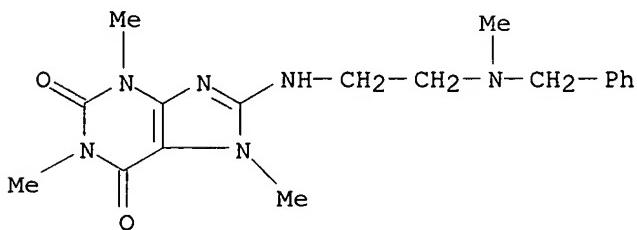
RN 33236-48-5 HCAPLUS

CN Caffeine, 8-[{2-[(m,.beta.-dihydroxyphenethyl)methylamino]ethyl}amino]- (8CI) (CA INDEX NAME)



RN 33236-49-6 HCAPLUS

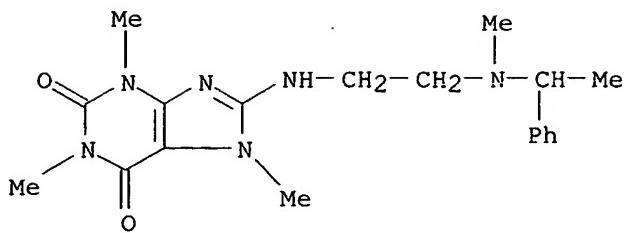
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[{2-[methyl(phenylmethyl)amino]ethyl}amino]- (9CI) (CA INDEX NAME)



RN 33236-50-9 HCAPLUS

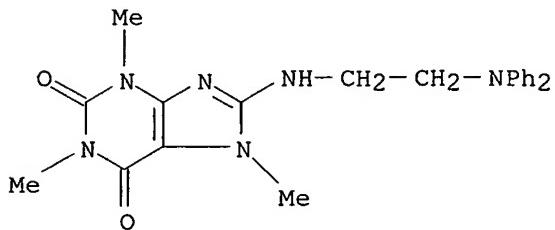
CN Caffeine, 8-[{2-[(methyl(.alpha.-methylbenzyl)amino)ethyl}amino]- (8CI)

(CA INDEX NAME)



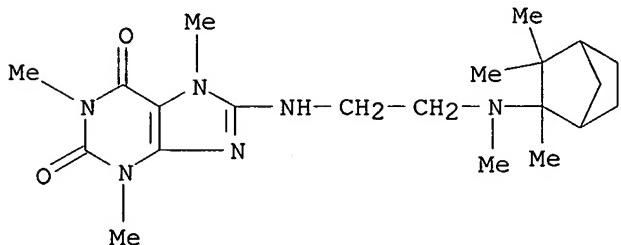
RN 33236-51-0 HCPLUS

CN Caffeine, 8-[(2-(diphenylamino)ethyl]amino]- (8CI) (CA INDEX NAME)



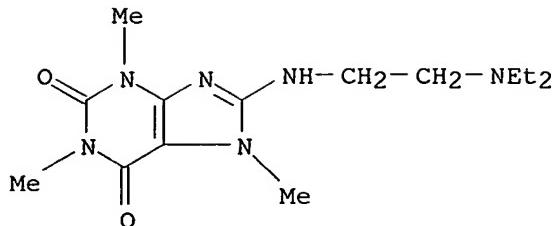
RN 33236-52-1 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(2,3,3-trimethylbicyclo[2.2.1]hept-2-yl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)



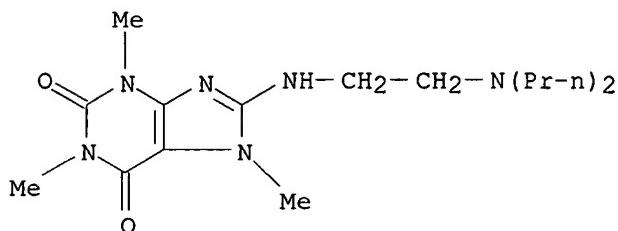
RN 33236-53-2 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(2-(diethylamino)ethyl]amino]-3,7-dihydro-1,3,7-trimethyl-, hydrochloride (9CI) (CA INDEX NAME)

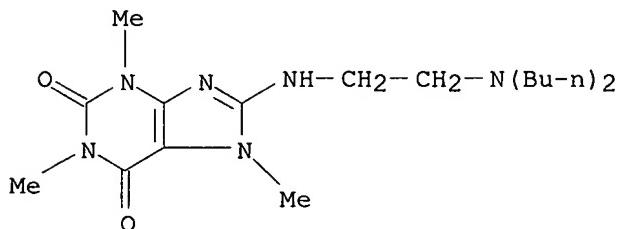


● x HCl

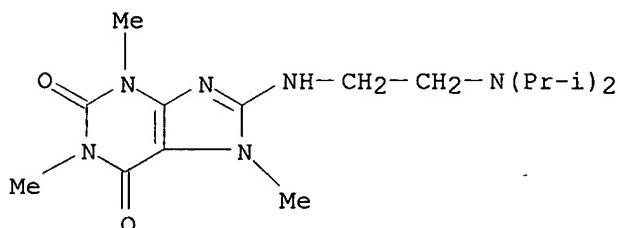
RN 33236-54-3 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[(2-(dipropylamino)ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 33236-55-4 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[(2-(dibutylamino)ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

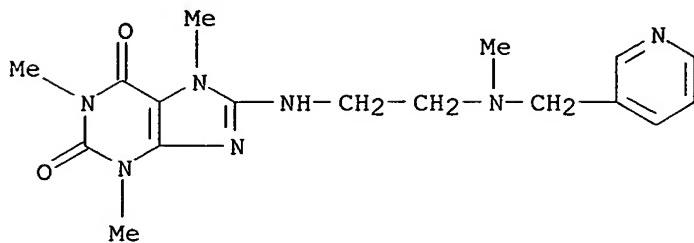


RN 33236-56-5 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[(2-[bis(1-methylethyl)amino]ethyl)amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



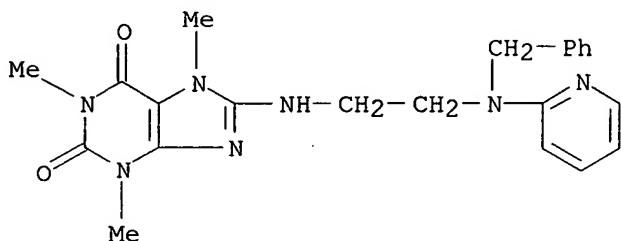
RN 33236-57-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(3-pyridinylmethyl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)



RN 33236-58-7 HCAPLUS

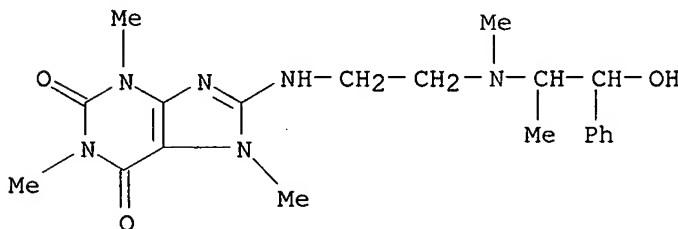
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[(phenylmethyl)-2-pyridinylamino]ethyl]amino]- (9CI) (CA INDEX NAME)



RN 33303-21-8 HCAPLUS

RN 33303-22-9 HCAPLUS

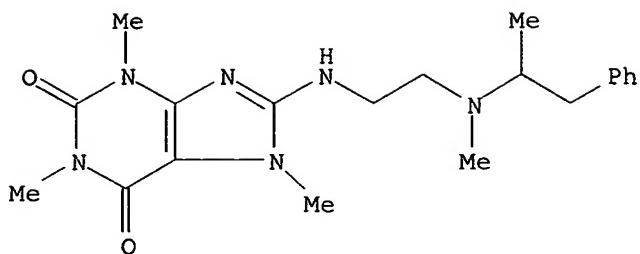
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(2-[(2-hydroxy-1-methyl-2-phenylethyl)methylamino]ethyl)amino]-1,3,7-trimethyl-, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

RN 33403-58-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[(2-[methyl(1-methyl-2-phenylethyl)amino]ethyl)amino]-, hydrochloride (9CI) (CA INDEX NAME)



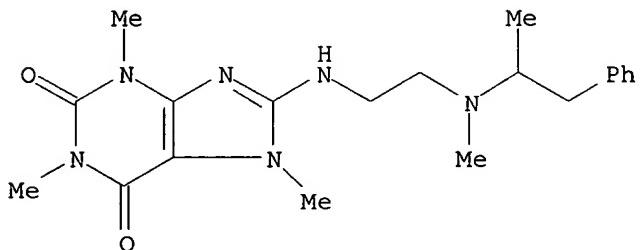
●x HCl

RN 33403-59-7 HCPLUS

RN 33403-60-0 HCPLUS

CN Caffeine, 8-[2-[methyl(.alpha.-methylphenethyl)amino]ethyl]amino]-, hydrochloride, (-)- (8CI) (CA INDEX NAME)

Rotation (-).



●x HCl

L23 ANSWER 23 OF 36 HCPLUS COPYRIGHT 2002 ACS

1971:418424 Document No. 75:18424 Trisubstituted ethylenediamines. 2. Pharmacological study of D, L-phencamine hydrochloride. Pitarch, L.; Iglesias, F.; Coronas, R. (Inst. Miquel Invest. Ter., Spain). Quim. Ind. (Madrid), 17(1), 76-81 (Spanish) 1971. CODEN: QUIBAL.

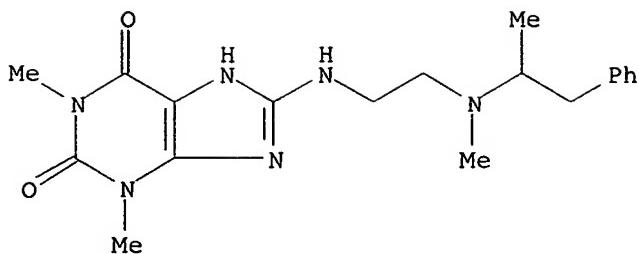
AB This compd., proposed as a psychotonic agent of the amphetamine type, did not produce anorexia or some of the other undesirable side effects. The acute i.p. LD<sub>50</sub> was 93 mg/kg in the rat and 82 mg/kg in the mouse. No teratogenic effect or chronic toxicity in effective doses was found.

IT 33001-55-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmacology of)

RN 33001-55-7 HCPLUS

CN Theophylline, 8-[2-[methyl(.alpha.-methylphenethyl)amino]ethyl]amino]-, hydrochloride, DL- (8CI) (CA INDEX NAME)



●x HCl

L23 ANSWER 24 OF 36 HCPLUS COPYRIGHT 2002 ACS

1970:477286 Document No. 73:77286 Physiologically active xanthine derivatives of ethylene diamine. (Instituto de Investigaciones Terapeuticas, S. A.). Brit. GB 1189617 19700429, 2 pp. (English). CODEN: BRXXAA. PRIORITY: ES 19671113 - 19680316 19680316.

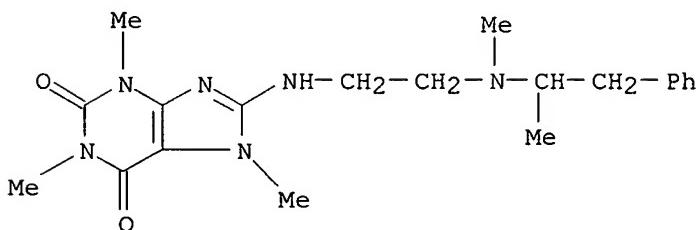
AB The analeptic, psychotonic, and antidepressive title compds. are prep'd. by treating an 8 (.beta.-haloethylamino)xanthine with an amine. Thus, 0.1 mole 8-(.beta.-chloroethylamino)caffeine, 0.1 mole methyl(.alpha.-methylphenethyl)-amine, 160 ml MeOH, and 0.05 mole K<sub>2</sub>CO<sub>3</sub> was refluxed 6 hr to give N-8-caffeyl-N'-methyl-N'-(.alpha.-methylphenethyl)ethylenediamine, m. 145.degree.; picrate m. 227.degree..

IT 28947-50-4

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmacology of)

RN 28947-50-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl-8-[[2-[methyl(1-methyl-2-phenylethyl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)



IT 28947-40-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

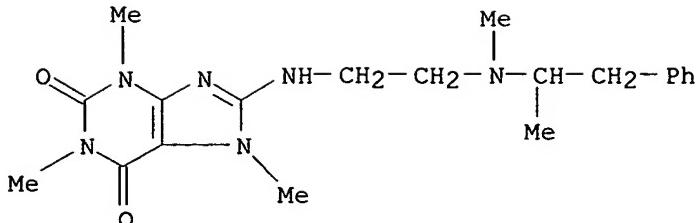
RN 28947-40-2 HCPLUS

CN Caffeine, 8-[[2-[methyl(.alpha.-methylphenethyl)amino]ethyl]amino]-, picrate (8CI) (CA INDEX NAME)

CM 1

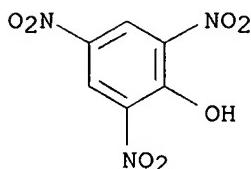
CRN 28947-50-4

CMF C20 H28 N6 O2



CM 2

CRN 88-89-1  
CMF C6 H3 N3 O7



L23 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1968:486959 Document No. 69:86959 8-Substituted derivatives of theophylline.  
Lespagnol, Albert; Tudo, Michele; Labiau, Odette; Robelet, Alfred;  
Bizard-Gregoire, N. (Lab. Pharm. Chim. Pharmacodyn., Fac. Med. Pharm.,  
Lille, Fr.). Ann. Pharm. Fr., 26(3), 207-14 (French) 1968. CODEN:  
APFRAD.

GI For diagram(s), see printed CA Issue.

AB 8-Substituted derivs. (I) of theophylline were prepd. and hypotensive and spasmolytic properties discussed. Thus, 20 g. bromotheophylline (II) was refluxed 20-4 hrs. with 20 g. (NH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub> and worked up to give I (R = NHCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>) HCl salt (III), m. 328-9.degree.. III (27 g.) was dissolved in a small amt. of hot alkalized H<sub>2</sub>O and 1 ml. BzH added dropwise to give after 24 hrs. 71% I (R = NHCH<sub>2</sub>CH<sub>2</sub>N:CHPh) (IV), m. 238-9.degree. (abs. alc.-dioxane). IV (5 g.) was converted to I (RNHCH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>Ph) (V), m. 170-2.degree., by Raney Ni redn. II (10 g.) was refluxed 1 hr. with 11.6 g. N,N-diethylenediamine to give 52% I (R = NHCH<sub>2</sub>CH<sub>2</sub>N<sub>2</sub>Et) (VI), m. 176.degree.; methiodide m. 239.degree.. I (R = NMeCH<sub>2</sub>CH<sub>2</sub>NMeCH<sub>2</sub>Ph) (VII), m. 158.degree., was prepd. by refluxing a mixt. of 23 g. HCO<sub>2</sub>H and 3.28 g. V with 3 ml. HCHO for 24 hrs.; methiodide m. 232.degree.. Substitution in the 8-position of I did not modify the hypotensive and spasmolytic properties. The derivs. prepd. have an important hypotensive activity and cause a spasmolytic action of the fibers similar to atropinic and papaverinic types.

IT 14251-33-3P 14317-02-3P 19899-51-5P

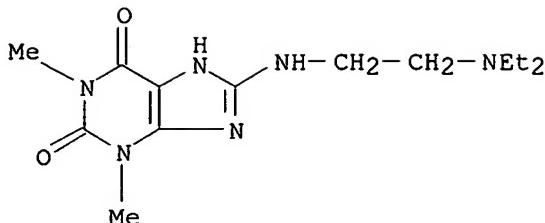
19899-52-6P 19899-53-7P 19899-56-0P

19899-57-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

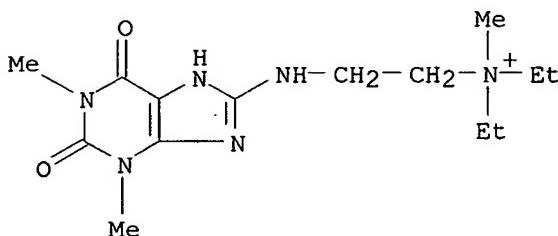
RN 14251-33-3 HCAPLUS

CN Theophylline, 8-[(2-(diethylamino)ethyl]amino]- (8CI) (CA INDEX NAME)



RN 14317-02-3 HCAPLUS

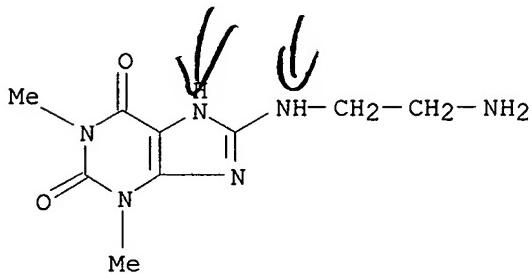
CN Ammonium, diethylmethyl[2-[(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]ethyl]-, iodide (8CI) (CA INDEX NAME)



● I<sup>-</sup>

RN 19899-51-5 HCAPLUS

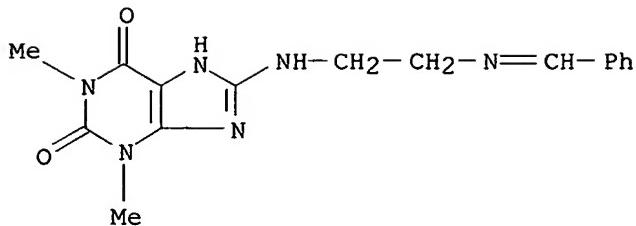
CN Theophylline, 8-[(2-aminoethyl)amino]-, monohydrochloride (8CI) (CA INDEX NAME)



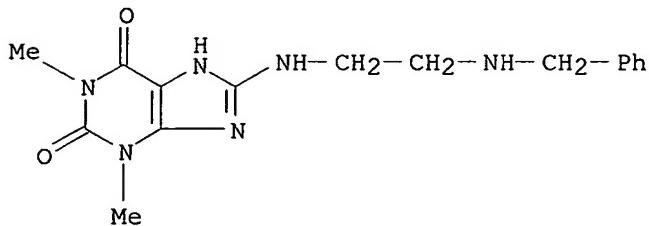
● HCl

RN 19899-52-6 HCAPLUS

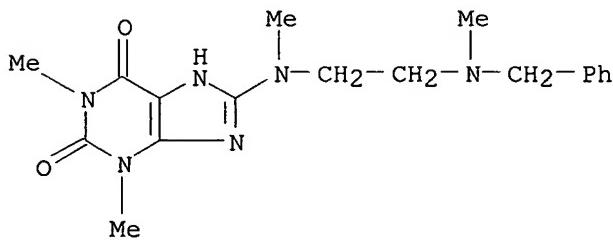
CN Theophylline, 8-[(2-(benzylideneamino)ethyl)amino]- (8CI) (CA INDEX NAME)



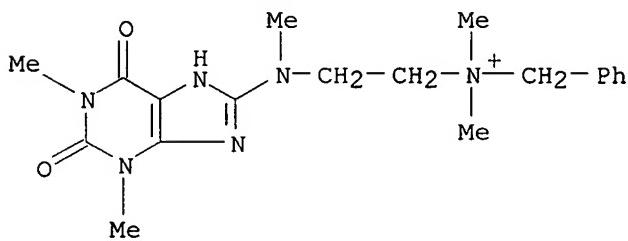
RN 19899-53-7 HCAPLUS  
 CN Theophylline, 8-[{2-(benzylamino)ethyl}amino]- (8CI) (CA INDEX NAME)



RN 19899-56-0 HCAPLUS  
 CN Theophylline, 8-[{2-(benzylmethylamino)ethyl}methylamino]- (8CI) (CA INDEX NAME)



RN 19899-57-1 HCAPLUS  
 CN Ammonium, benzyldimethyl[2-[methyl(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]ethyl]-, iodide (8CI) (CA INDEX NAME)



● I-

L23 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1967:420141 Document No. 67:20141 Pharmacological effects of some 8-substituted theophylline derivatives. Robelet, Alfred; Dezeustre, J.; Leroy, Albert; Bizard, Jacques (Univ. Lille, Lille, Fr.). J. Physiol. (Paris), 57, 689-90 From: CZ 1966, (47), Abstr. No. 1736 (French) 1965. CODEN: JOPHAN.

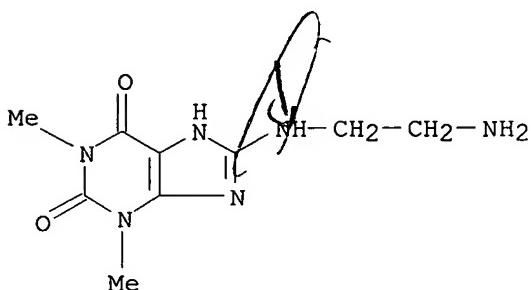
AB The blood and pressure lowering and spasmolytic effect of theophylline was not basically changed by the substitution of an amino side chain in the 8-position, nor was it increased or decreased by a quaternary ammonium group when the side chain contained a primary amine group at the C-8 position. 8-[.beta.-Aminoethylamino]-, 8-[.beta.- (diethylamino)ethylamino]-, and 8-[.beta.- (methyldiethylammonio)ethylamino]theophylline were tested.

IT 14251-32-2 14251-33-3 16806-01-2

RL: BIOL (Biological study)  
(antispasmodic and hypotensive activities of)

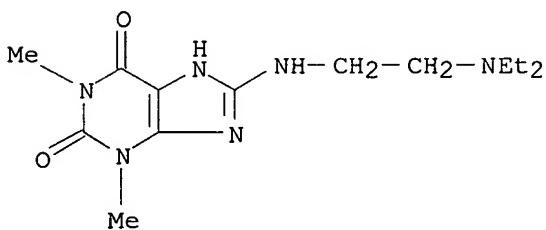
RN 14251-32-2 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-aminoethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



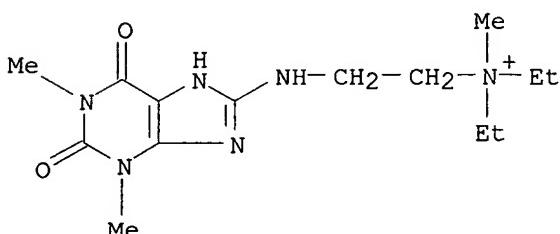
RN 14251-33-3 HCAPLUS

CN Theophylline, 8-[(2-(diethylamino)ethyl)amino]- (8CI) (CA INDEX NAME)



RN 16806-01-2 HCAPLUS

CN Ammonium, diethylmethyl[2-[(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]ethyl]- (8CI) (CA INDEX NAME)



L23 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1967:17883 Document No. 66:17883 Action of 8-substituted theophylline derivatives on the biliary tract. Bizard, Gaston; Bizard-Gregoire, N. (Univ. Lille, Lille, France). Arch. Ital. Sci. Farmacol., 15(1-2), 41-5 (French) 1965. CODEN: AISFAR.

GI For diagram(s), see printed CA Issue.

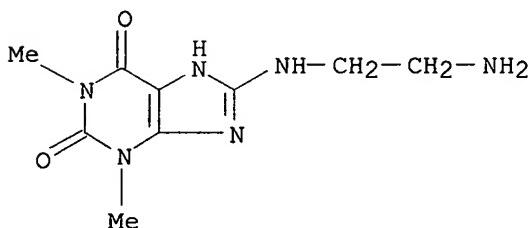
AB Some new theophylline (I, R = H) (Ia) derivs. were synthesized and tested for spasmolytic action on the biliary tract. The following I were investigated: R = NH(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub> (Ib), R = NH(CH<sub>2</sub>)<sub>2</sub>NET<sub>2</sub> (Ic), R = NH(CH<sub>2</sub>)<sub>2</sub>NEt<sub>2</sub>MeI (Id). The effects of the I drugs were investigated on the perfused biliary tract of the guinea pig *in situ*; the drugs were administered intravenously (25 mg./kg.). The effect on the above prepn., after previous contraction with morphine (5 mg./kg.), were also studied. In a 2nd series of expts., the influence of I on isolated guinea pig gall bladder, contracted by pretreatment with acetylcholine (10<sup>-7</sup>M) was detd. In both tests, Ib and Ic showed the same spasmolytic action as Ia, whereas Id was inactive.

IT 14251-32-2 14251-33-3 14317-02-3

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
(biliary tract response to)

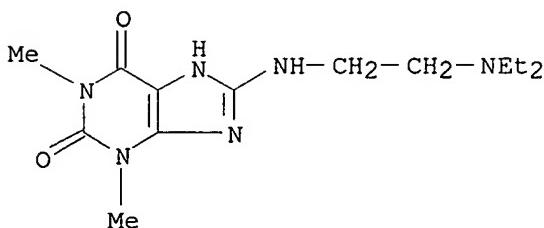
RN 14251-32-2 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-aminoethyl)amino]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



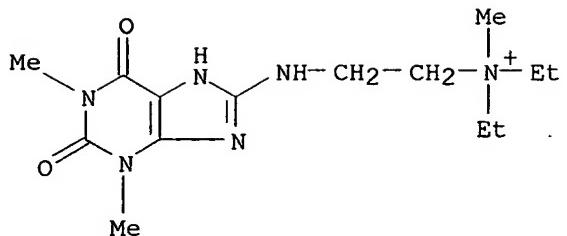
RN 14251-33-3 HCAPLUS

CN Theophylline, 8-[(2-(diethylamino)ethyl]amino]- (8CI) (CA INDEX NAME)



RN 14317-02-3 HCAPLUS

CN Ammonium, diethylmethyl[2-[(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]ethyl]-, iodide (8CI) (CA INDEX NAME)



● I<sup>-</sup>

L23 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2002 ACS

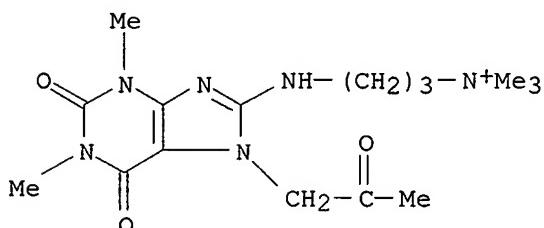
1965:51642 Document No. 62:51642 Original Reference No. 62:9130d-e Some purine azides. Smirnova, N. B.; Postovskii, I. Ya. (S. M. Kirov Polytech. Inst., Sverdlovsk). Zh. Vses. Khim. Obshchestva im. D. I. Mendeleva, 9(6), 711-12 (Russian) 1964.

AB 2,6-Dichloropurine and NaN<sub>3</sub> refluxed 5 min. in aq. EtOH gave 75% 2,6-diazidopurine (I), decompd. 190-200.degree.; similarly was prep'd. 2,6,8-triazidopurine, decompd. 180-90.degree.. I refluxed 1 hr. in aq. piperidine gave 82% 6-(N-piperidinyl)-2-azidopurine, decompd. 215-16.degree.. Similarly were prep'd. 6-morpholino-2-azidopurine, decompd. about 260.degree., 6-(N-piperidinyl)-2,8-diazidopurine, decompd. 190-200.degree., and 6-morpholino-2,8-diazidopurine, decompd. 190-200.degree.. Uv spectra of the products were reported

IT 977-77-5, Ammonium, [3-[(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]propyl]trimethyl, bromide (prepn. of)

RN 977-77-5 HCAPLUS

CN Ammonium, [3-[(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]propyl]trimethyl-, bromide (8CI) (CA INDEX NAME)



● Br<sup>-</sup>

L23 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1965:51641 Document No. 62:51641 Original Reference No. 62:9130c-d Synthesis in the theophylline series. XI. Synthesis of 7-acetonyltheophyllines. J. Prakt. Chem., 26(3-4), 155-8 (Unavailable) 1964.

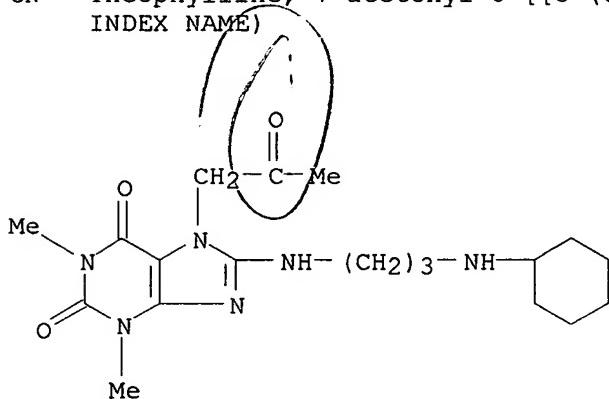
AB I or the Br analog with dialkylaminoalkylamines yielded the corresponding II under mild conditions. I (27 g.) and 11.6 g. Et<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> in 100 cc.

iso-PrOH refluxed 5 hrs. yielded 25 g. II (R = H, R<sub>1</sub> = CH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>) (V), m. 143-5.degree. (repptd. from MePh with petr. ether); V. HCl m. 288-90.degree.; V. MeBr m. 297-9.degree.. Similarly were prep'd. the following II (R, R<sub>1</sub>, and m.ps. of base and HCl salt given): H, Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>, 118-20.degree., 260-2.degree. (methobromide m. 238-40.degree.); H, Me<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>, 125-7.degree., 240-2.degree. (methobromide m. 225-7.degree.); Me, Et<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>, 98, -- (hygroscopic); Me, Me<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>, 114-16.degree., 254-6.degree.; H, 2-piperidinoethyl, 158-60.degree., --; H, 2-morpholinoethyl, 198-200.degree., 266-8.degree.; H, 3-cyclohexylaminopropyl, 120-2.degree., 325-7.degree.. Similarly was prep'd. II [(R<sub>1</sub> = ) 4-methylpiperazino)], m. 135-7.degree.; HCl salt m. 272-4.degree.. II did not reach the pharmacol. activity of theophylline, caffeine, or 7-acetonyltheophylline.

IT 910-46-3, Theophylline, 7-acetonyl-8-[(3-(cyclohexylamino)propyl)amino]- 977-77-5, Ammonium, [3-[(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]propyl]trimethyl, bromide 99888-39-8, Theophylline, 7-acetonyl-8-[(3-(cyclohexylamino)propyl)amino]-, hydrochloride (prep'n. of)

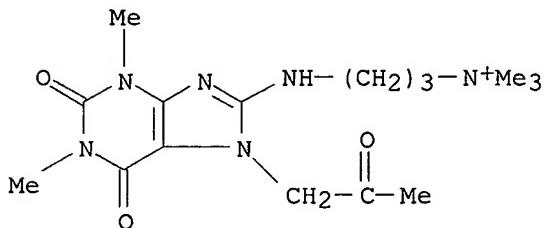
RN 910-46-3 HCPLUS

CN Theophylline, 7-acetonyl-8-[(3-(cyclohexylamino)propyl)amino]- (8CI) (CA INDEX NAME)



RN 977-77-5 HCPLUS

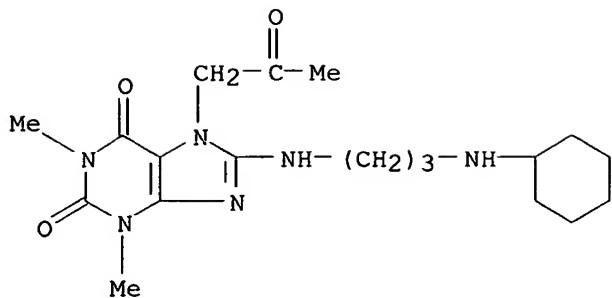
CN Ammonium, [3-[(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]propyl]trimethyl-, bromide (8CI) (CA INDEX NAME)



● Br<sup>-</sup>

RN 99888-39-8 HCPLUS

CN Theophylline, 7-acetonyl-8-[(3-(cyclohexylamino)propyl)amino]-, hydrochloride (7CI) (CA INDEX NAME)



● x HCl

L23 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1965:51640 Document No. 62:51640 Original Reference No. 62:9129h, 9130a-c  
Synthesis in the theophylline series. X. Syntheses of xanthine amino acids. Klosa, Josef J. Prakt. Chem., 26(1-2), 48-53 (German) 1964.

GI For diagram(s), see printed CA Issue.

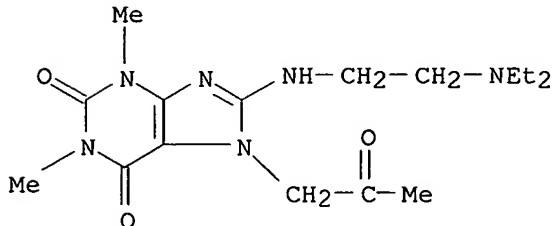
AB cf. CA 55, 5511d. 7-Acetonyl-8-chlorotheophylline (I) or the Br analog was converted with amino acids in the presence of alkali into the corresponding 7-acetonyl-8-thiophyllinylamino acids. I (27 g.) in 60 cc. H<sub>2</sub>O treated with stirring with 10 g. H<sub>2</sub>NCH<sub>2</sub>CO<sub>2</sub>H and adjusted with 2N NaOH to pH 8-9, refluxed with stirring while being maintained at pH 7.5-8.5 by the dropwise addn. of 2N NaOH, and refluxed an addnl. hr. yielded 32 g. II (R = NHCH<sub>2</sub>CO<sub>2</sub>H, R<sub>1</sub> = H) (III), m. 294-6.degree. (decompn.) with browning from 260.degree.. III dissolved in an equiv. amt. aq. 50% NaOH and dild. with EtOH yielded the Na salt of III, m. >330.degree. (decompn.). III (6.2 g.) and 4 g. L-ephedrine (IV) refluxed in MeOH to soln. and cooled gave 9 g. III-IV salt, m. 218-20.degree.. Similarly were prep'd. the following II (R<sub>1</sub> = H) (R, m.p., and % yield given): CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H, 270-2.degree., 85; CHMeCO<sub>2</sub>H, 233-5.degree., 70; PhCHCO<sub>2</sub>H, 145-7.degree., 60; PhCH<sub>2</sub>CHCO<sub>2</sub>H, 230-2.degree., 70; p-HOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CHCO<sub>2</sub>H, 258-60.degree., 60; EtCHCO<sub>2</sub>H, 215-17.degree., 60; MeCHCH<sub>2</sub>CO<sub>2</sub>H, 254-6.degree., 55; (CH<sub>2</sub>)<sub>3</sub>CO<sub>2</sub>H, 236-8.degree., 45; (CH<sub>2</sub>)<sub>5</sub>CO<sub>2</sub>H, 226-8.degree., 65; iso-PrCHCO<sub>2</sub>H, 204-6.degree., 40; EtMeCCO<sub>2</sub>H, 223-5.degree., 45; iso-BuCHCO<sub>2</sub>H, 126-8.degree., 60; HO<sub>2</sub>CCHCH<sub>2</sub>CO<sub>2</sub>H, 228-30.degree. (aq. MeOH), 85; HO<sub>2</sub>CCHCH<sub>2</sub>CONH<sub>2</sub>, 258-60.degree. (85% iso-PrOH), 85; HO<sub>2</sub>CCH<sub>2</sub>CH<sub>2</sub>CHCO<sub>2</sub>H, 102-4.degree. (aq. MeOH), 80; H<sub>2</sub>NOCCH<sub>2</sub>CH<sub>2</sub>CHCO<sub>2</sub>H, 263-5.degree. (90% iso-PrOH), 80; MeSCH<sub>2</sub>CH<sub>2</sub>CHCO<sub>2</sub>H, 194-6.degree., 75. II did not exhibit any pharmacol. activity; their L.D.50 values are above 3 g. orally. The III-IV salt is not only more toxic than III, but it exhibited also a 30% increase of the hypotensive activity of IV with considerable prolongation of the effect.

IT 855-44-7, Theophylline, 7-acetonyl-8-[(2-(diethylamino)ethyl]amino]- 857-33-0, Asparagine, N<sub>2</sub>-(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)- 858-86-6, Glutamine, N<sub>2</sub>-(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)- 907-30-2, Theophylline, 7-acetonyl-8-[(3-(diethylamino)propyl]amino]- 909-25-1, Ammonium, [3-[(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]propyl]diethylmethyl, bromide 1046-21-5, Theophylline, 7-acetonyl-8-[(3-(dimethylamino)propyl]amino]- 1101-57-1, Ammonium, [2-[(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]ethyl]diethylmethyl, bromide 97811-60-4, Theophylline, 7-acetonyl-8-[(2-(diethylamino)ethyl]amino]-, hydrochloride

**98468-17-8**, Theophylline, 7-acetyl-8-[(3-(diethylamino)propyl)amino]-, hydrochloride  
(prepn. of)

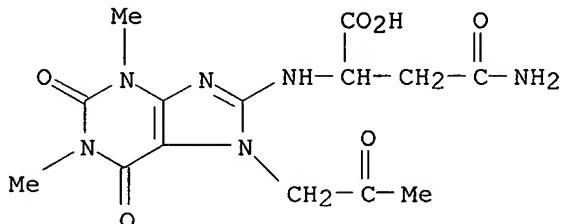
RN 855-44-7 HCAPLUS

CN Theophylline, 7-acetyl-8-[(2-(diethylamino)ethyl)amino]- (7CI, 8CI) (CA INDEX NAME)



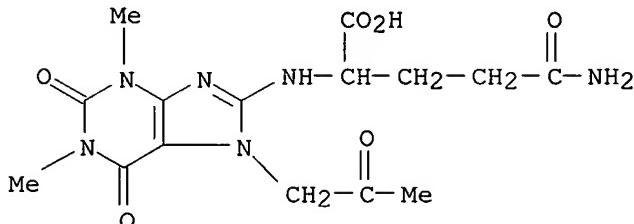
RN 857-33-0 HCAPLUS

CN Asparagine, N2-(7-acetyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)- (7CI, 8CI) (CA INDEX NAME)



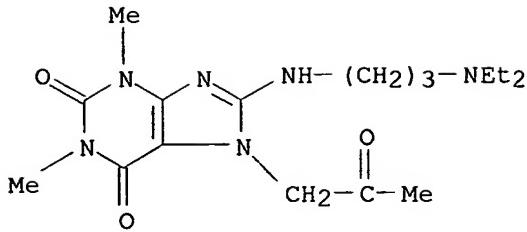
RN 858-86-6 HCAPLUS

CN Glutamine, N2-(7-acetyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)- (7CI, 8CI) (CA INDEX NAME)

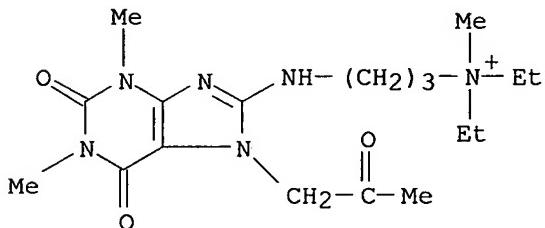


RN 907-30-2 HCAPLUS

CN Theophylline, 7-acetyl-8-[(3-(diethylamino)propyl)amino]- (7CI, 8CI)  
(CA INDEX NAME)

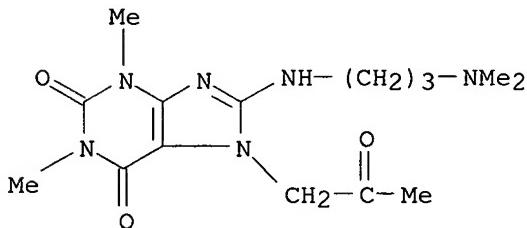


RN 909-25-1 HCAPLUS  
 CN Ammonium, [3-[(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]propyl]diethylmethyl-, bromide (8CI) (CA INDEX NAME)

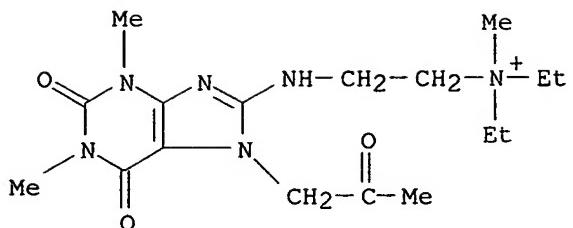


● Br<sup>-</sup>

RN 1046-21-5 HCAPLUS  
 CN Theophylline, 7-acetonyl-8-[(3-(dimethylamino)propyl)amino]- (7CI, 8CI) (CA INDEX NAME)



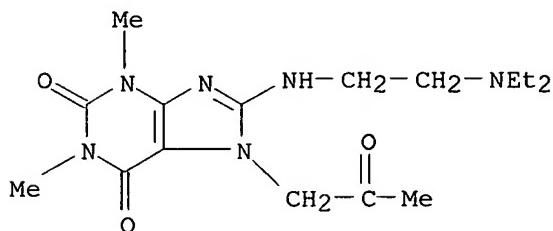
RN 1101-57-1 HCAPLUS  
 CN Ammonium, [2-[(7-acetonyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)amino]ethyl]diethylmethyl-, bromide (8CI) (CA INDEX NAME)



● Br<sup>-</sup>

RN 97811-60-4 HCPLUS

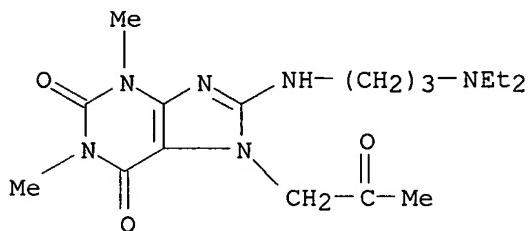
CN Theophylline, 7-acetonyl-8-[(2-(diethylamino)ethyl)amino]-, hydrochloride  
(7CI) (CA INDEX NAME)



●x HCl

RN 98468-17-8 HCPLUS

CN Theophylline, 7-acetonyl-8-[(3-(diethylamino)propyl)amino]-, hydrochloride  
(7CI) (CA INDEX NAME)



●x HCl

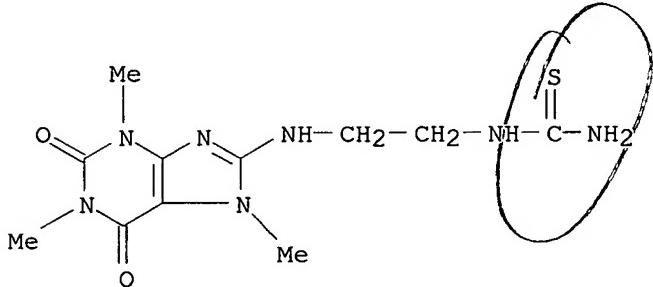
L23 ANSWER 31 OF 36 HCPLUS COPYRIGHT 2002 ACS

1964:484254 Document No. 61:84254 Original Reference No. 61:14674a-d

Sulfur-containing derivatives of purines and pyrimidines. Lyashenko, V. D.; Kolesova, M. B.; Aleksandr, Kh. L.; Sheremet'eva, V. A. (Chem.-Pharm. Inst., Leningrad). Zh. Obshch. Khim., 34(8), 2752-6 (Unavailable) 1964.

AB Heating 4-methyluracil with ClCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> and paraformaldehyde in Me<sub>2</sub>NCHO 1

hr. at 110.degree. gave 20% 4-methyl-5-(2-chloroethylamino)methyluracil-HCl, m. 273.degree.. Similarly was prep'd. 5-(2-chloroethylamino)methyluracil-HCl, decompd. above 260.degree.. Refluxing 8-halopurines with HOCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> gave 8-(2-hydroxyethyl)aminotheophylline-HBr, decompd. 300.degree., 8-(2-hydroxyethyl)aminotheobromine-HBr, decompd. 318.degree., and 8-(2-hydroxyethyl)aminocaffeine-HBr, decompd. 300.degree.. Heating these with SC(NH<sub>2</sub>)<sub>2</sub> in excess 48% HBr gave the following RNHCH<sub>2</sub>CH<sub>2</sub>SC(:NH)NH<sub>2</sub>.2HBr (R and decompn. point given): adenin-8-yl, 275.degree.; theophyllin-8-yl, 315.degree.; caffein-8-yl, 241.degree.; theobromin-8-yl, 283.degree.. 9-(.beta.-Chloroethyl)adenine heated with aq. SC(NH<sub>2</sub>)<sub>2</sub> gave adenin-9-yethyliothiuronium chloride. 8-Chlorotheobromine refluxed with aminoethylisothiuronium chloride in alc. NaOH 12 hrs. gave 38.6% 8-(2-guanidinoethyl)thiotheobromine-HCl, decompd. 305.degree.. 2-Mercaptoadenine and ClCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>.HCl in 2N NaOH 2 hrs. at 90.degree. gave 2-(2-aminoethyl)thioadenine-HCl, m. 198-200.degree.. 8-Bromoadenine and cystamine-HCl in aq. NaOH-Et<sub>3</sub>N gave after 3 hrs. at 160-70.degree. in a sealed tube 52.5% N,N'-di(8-adeninyl)cystamine, decompd. above 200.degree.. The following thiuronium salts were prep'd. from corresponding chloro derivs. and aq. SC(NH<sub>2</sub>)<sub>2</sub>: 2,6-dihydroxy-4-methyl-5-pyrimidylmethylisothiuronium chloride, m. 223.degree.; 2,6-dihydroxy-4-methyl-5-pyrimidinylmethylaminoethylisothiuronium chloride, m. 273.degree.; and 2,6-dihydroxy-5-pyrimidinylmethylaminoethylisothiuronium chloride, decompd. 250.degree.. The homogeneity of the products was confirmed by paper chromatography  
 IT 94584-65-3, Pseudourea, 2-[2-[(1,2,3,6-tetrahydro-1,3,7-trimethyl-2,6-dioxopurin-8-yl)amino]ethyl]-2-thio-, hydrobromide  
 (prep'n. of)  
 RN 94584-65-3 HCPLUS  
 CN Pseudourea, 2-[2-[(1,2,3,6-tetrahydro-1,3,7-trimethyl-2,6-dioxopurin-8-yl)amino]ethyl]-2-thio-, hydrobromide (7CI) (CA INDEX NAME)



● HBr

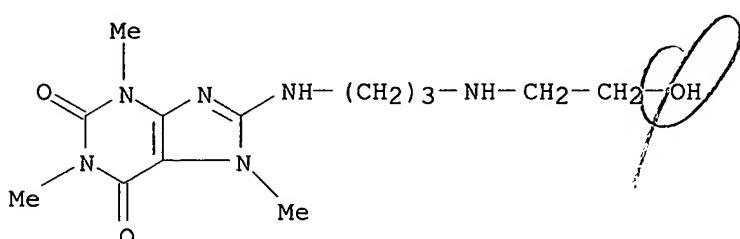
L23 ANSWER 32 OF 36 HCPLUS COPYRIGHT 2002 ACS  
 1963:475376 Document No. 59:75376 Original Reference No. 59:14004a-d  
 8-Caffeinylalkylenediamines. Klosa, Josef (Delmar Chemicals Ltd.). US  
 3094529 19630618, 3 pp. (Unavailable). APPLICATION: US 19590911.  
 GI For diagram(s), see printed CA Issue.  
 AB The title compds. (I) have a strong and sustained hypotensive action. Thus, 0.1 mole .beta.-(8-caffeinyl)aminoethyl chloride and 0.2 mole piperidine were refluxed with 40 ml. alc. 8 hrs. and cooled, the solid filtered off and dissolved in H<sub>2</sub>O, and the soln. made strongly alk. to give 1-piperidino-2-(8-caffeinyl)aminoethylene, m. 198-200.degree. (alc.); hydrochloride, m. 178-80.degree., 225-7.degree., and 268.degree. (decompn.). Similarly, prep'd. were I (R, n, R', and m.p. given): H, morpholino, 2, 181-3.degree. (alc.) (hydrochloride m. 220-2.degree.);

dihydrochloride m. 170.degree. and 247-9.degree.); H, pyrrolidino, 3, 184-5.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether); H, NHPh, 3, 159-61.degree. (alc.); H, NHCHMeCH<sub>2</sub>Ph, 3, 163-5.degree. (alc.). By another method, 11 g. 8-chlorocaffeine was mixed with 8 ml. N-(hydroxyethyl)propylenediamine at 140-60.degree.; the temp. rose to 180.degree.. The mixt. was heated 0.5 hr., the solidified mass heated 10 min., cooled, and taken up in alc., an equal vol. H<sub>2</sub>O added, the soln. made strongly alk. the milky cloudiness solidified on cooling to give I (R = H, R<sub>1</sub> = NHCH<sub>2</sub>CH<sub>2</sub>OH, n = 3) m. 175-7.degree. (H<sub>2</sub>O). Similarly prep'd. were I (R, R', n, and m.p. given): H, NHCH<sub>2</sub>CH<sub>2</sub>OH, 2, 195-7.degree.; H, N(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>, 2, 142-4.degree..

IT 96635-36-8, Caffeine, 8-[{3-[(2-hydroxyethyl)amino]propyl}-amino]-  
97302-64-2, Caffeine, 8-[{2-[bis(2-hydroxyethyl)amino]ethyl}-amino]-  
98146-24-8, Caffeine, 8-[{(3-anilinopropyl)amino]-  
100150-05-8, Caffeine, 8-[{3-[(.alpha.-methylphenethyl)amino]propyl}amino]-  
(prepn. of)

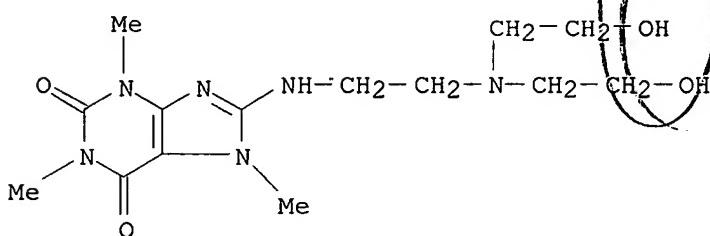
RN 96635-36-8 HCPLUS

CN Caffeine, 8-[{3-[(2-hydroxyethyl)amino]propyl}amino]- (7CI) (CA INDEX NAME)



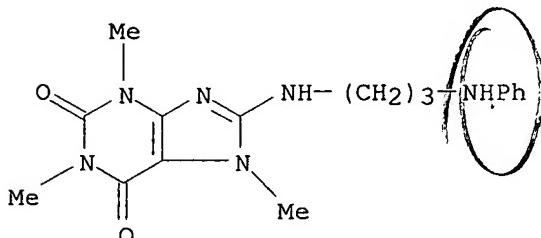
RN 97302-64-2 HCPLUS

CN Caffeine, 8-[{2-[bis(2-hydroxyethyl)amino]ethyl}amino]- (7CI) (CA INDEX NAME)

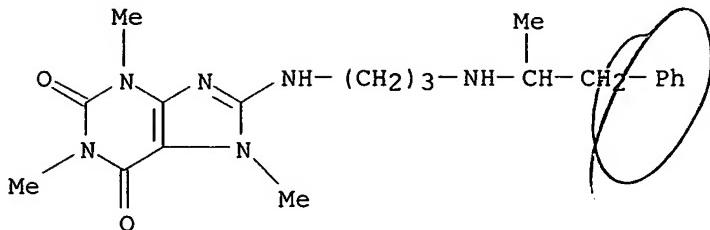


RN 98146-24-8 HCPLUS

CN Caffeine, 8-[{(3-anilinopropyl)amino]- (7CI) (CA INDEX NAME)



RN 100150-05-8 HCPLUS  
CN Caffeine, 8-[{3-[({.alpha.-methylphenethyl)amino]propyl}amino]- (7CI) (CA INDEX NAME)



L23 ANSWER 33 OF 36 HCPLUS COPYRIGHT 2002 ACS

1963:448356 Document No. 59:48356 Original Reference No. 59:8738d-g  
Potential anticancer compounds. III. Synthesis of some 8-substituted  
caffees and theophyllines. Zimmer, Hans; Metallia, Joseph B., Jr.;  
Atchley, R. (Univ. of Cincinnati, Cincinnati, OH). Ohio J. Sci., 63,  
97-102 (Unavailable) 1963.

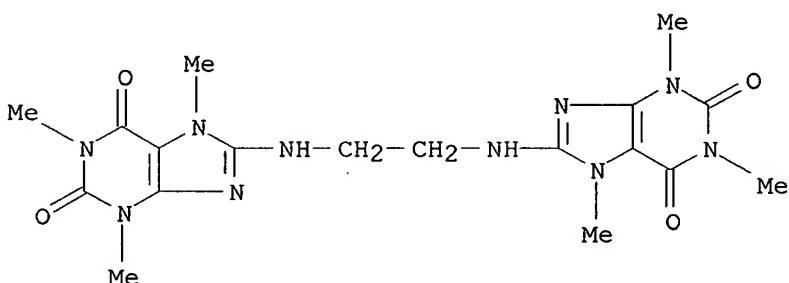
GI For diagram(s), see printed CA Issue.

AB cf. CA 54, 4368c, 5447f. The following I were prep'd. by refluxing  
8-bromocaffeine with alkylamines in BuOH for 17 hrs. (R, % yield, and m.p.  
given): PrNH, 82, 238-40.degree.; BuNH, 85, 225-7.degree.; n-C<sub>6</sub>H<sub>13</sub>NH, 75,  
195-6.degree.; iso-PrNH, 57, 241-3.degree.; sec-BuNH 27, 216-18.degree.;  
morpholino, 74, 166.degree.; p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>NH, 0.5, >320.degree.; HNCH<sub>2</sub>CH<sub>2</sub>NH  
(bis), 67, >320.degree.; HOCH<sub>2</sub>CH<sub>2</sub>NH, 90, 232-4.degree.; (HOCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N, 44,  
138-9.degree. (124-6.degree.); (ClCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N, 52, 151-3.degree. (decompn.);  
tert-BuNHCH<sub>2</sub>, 30, 189-91.degree.; (EtO)<sub>2</sub>-CHCH<sub>2</sub>NH, 61.5, 183.4.degree.  
(decompn.). Also prep'd. were 8-bis(2-hydroxyethyl)aminothephylle, 64%  
yield, m. 246-8.degree., and the 2-chloroethyl analog, 57% yield, m.  
(177.degree.) 205-8.degree.. Treatment of I with HNO<sub>2</sub> or NOCl gave the  
corresponding 8-(N-nitroso) deriv. of I (R, % yield, and m.p. given):  
N(NO)Et, 52-6, 106-8.degree.; N(NO)Bu, 47-58, 77-9.degree.; N(NO)C<sub>6</sub>H<sub>13</sub>-n,  
91, 53-5.degree.; N(NO)CH<sub>2</sub>CH<sub>2</sub>N(NO), 58, >320.degree.. Also prep'd. were  
8-(p-nitrobenzylidene)aminocaffeine, 22% yield, m. 300-2.degree.  
(decompn.), and the 8-(p-dimethylaminobenzylidene) analog, m.  
297-9.degree.. Possible tautomeric structures of I were discussed in  
terms of infrared and ultraviolet spectra. The compds. showed no  
carcinogenic activity.

IT 98691-97-5, Caffeine, 8,8'-(ethylenediamino)di-  
(prepn. of)

RN 98691-97-5 HCPLUS

CN Caffeine, 8,8'-(ethylenediamino)di- (6CI, 7CI) (CA INDEX NAME)



L23 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1963:409047 Document No. 59:9047 Original Reference No. 59:1658f-g

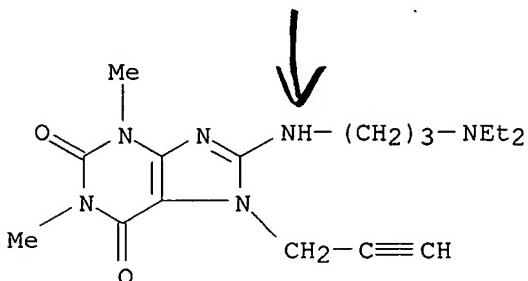
7,8-Substituted theophyllines. Nakanishi, Michio (Yoshitomi Pharmaceutical Industries, Ltd.). JP 37004895 19620616 Showa, 2 pp. (Unavailable). APPLICATION: JP 19590818.

AB A mixt. of 4.5 g. morpholine, 17 g. 8-bromo-7-propyn-2-yltheophylline, 4.5 g. K<sub>2</sub>CO<sub>3</sub>, and 150 cc. EtOH is refluxed for 7 hrs. to give 8-morpholino-7-propyn-2-yltheophylline, m. 174.degree. (EtOH). Similarly prepd. are the following 7-propyro-2-yl-7-(R-substituted) theophyllines. (R and m.p. given): piperidino, 183.degree.; Et<sub>2</sub>N, 92.degree.; N-methyl-N'-piperazino, 146.degree.; 2-phenylisopropylamino, 234-5.degree.; 3-(2-ethylhexyloxy)propylamino, 136-7.degree.; 3-diethylaminopropylamino, 184-5.degree.; .gamma.-[.beta.-(.beta.-hydroxyethoxy)ethoxy]propylamino, 151.degree.; .gamma.-morpholinopropylamino, 156.degree.. The compds. are useful as diuretics and cardiotonics.

IT 98147-52-5, Theophylline, 8-[{3-(diethylamino)propyl}amino]-7-(2-propynyl)- (prepn. of)

RN 98147-52-5 HCAPLUS

CN Theophylline, 8-[{3-(diethylamino)propyl}amino]-7-(2-propynyl)- (7CI) (CA INDEX NAME)



L23 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2002 ACS

1963:33375 Document No. 58:33375 Original Reference No. 58:5670g-h,5671a-e

Caffeine-8-alkylene diamines. Klosa, Josef (Privat-Lab., Berlin Zehlendorf, Germany). J. Prakt. Chem., 18, 97-106 (Unavailable) 1962.

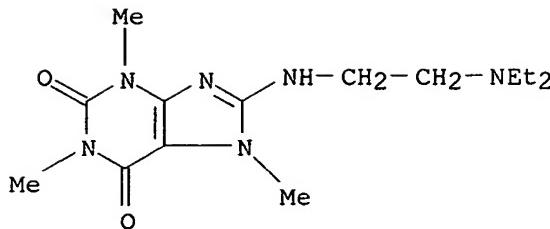
AB The title compds. were prepd. by reaction of 8-chloro- or 8-bromocaffeine (I or II) and alkylendiamines or by treatment of 8-(.beta.-chloroalkyl)alkylamino- or aminocaffeine with primary or secondary bases. 8-(.beta.-Hydroxyethyl)aminocaffeine (10 g.) was added in portions to 10 ml. SOCl<sub>2</sub>, the mixt. heated 20-30 min. on a steam bath, and washed many times with refluxing C<sub>6</sub>H<sub>6</sub> to give 11 g. 8-(.beta.-chloroethyl)aminocaffeine (III), m. 225-7.degree. (MeOH). Similarly, 50 g. 8-(.gamma.-hydroxypropyl)amino-caffeine and 100 ml. SOCl<sub>2</sub>. gave 55 g. 8-(.beta.-chloropropyl)aminocaffeine (IV), m. 210-12.degree. (EtOH), and 40 g. 8-(.beta.-hydroxyethyl)-methylaminocaffeine and 40 ml. SOCl<sub>2</sub> refluxed 2 hrs. and then n2poured onto ice and neutralized with dil. NH<sub>3</sub> gave 8-(.beta.-chloroethyl)methylaminocaffeine (V). I (22 g.) and 23 g. Et<sub>2</sub>NCH<sub>2</sub>-CH<sub>2</sub>NH<sub>2</sub> were rubbed together, heated to 140.degree. to effect soln., and then refluxed 20 min. at 150-70.degree.. The mixt. was cooled, dissolved in hot EtOH, cooled, and filtered and the crystals dissolved in EtOH, treated with HCl-EtOH, and then with double the vol. of Et<sub>2</sub>O to give 80% N,N-diethyl-N'-(caffein-8-yl)ethylenediamine hydrochloride, m. 288-90.degree.; free base m. 186-8.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether); methobromide m. 230.degree.. I (44 g.) and 42 ml. Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>NH<sub>2</sub> heated a few min. at 160-70.degree. gave a mixt. which soon solidified and was

purified by washing twice with refluxing EtOH, pptg. 80%  
N,N-diethyl-N'-(cafein-8-yl)trimethylenediamine hydrochloride, m.  
222-4.degree. (Et-OH-Et2O); free base m. 158-60.degree. (C6H6-petr. ether  
or PhMe-petr. ether); methobromide m. 226.degree.; methiodide m.  
244-6.degree. (MeOH). The following compds. were similarly prep'd.  
(product, % yield, m.p., crystn. solvent; hydrochloride m.p. given):  
N,N-dimethyl-N'-(cafein-8-yl)trimethylenediamine, 75-80, 173-5.degree.,  
C6H6-petr. ether, 268-70.degree.; N-cyclohexyl-N'-(cafein-8-yl)-  
trimethylenediamine, --, 136-8.degree., C6H6-petr. ether, 240-2.degree.  
(dihydrochloride m. 240.degree.); N-methyl-N-(cafein-8-yl)-N',N'-  
diethylenediamine, --, 145-7.degree., --, N-ethyl-N-(cafein-8-  
yl)-N',N'-diethylenediamine, --, 138-40.degree., C6H6-petr. ether,  
--. V (28 g.), 10 ml. pyrrolidine, and 8 g. anhyd. K2CO3 was refluxed 5-6  
hrs. in 250 ml. 96% EtOH and the soln. filtered hot and reduced to half  
vol. to give 22 g. 1-(cafein-8-yl)methylamino-2-pyrrolidinoethane, m.  
70-2.degree. (C6H6-petr. ether). The following compds. were similarly  
prep'd. from I, III, or IV and the appropriate amines (product, m.p.,  
crystn. solvent, hydrochloride m.p. given): 1-piperidino-2-(cafein-8-yl)-  
ethane, 198-200.degree., EtOH, 268.degree. (decompn.);  
1-morpholino-2-(cafein-8-yl)ethane, 181-3.degree., EtOH, 220-2.degree.  
[dihydrochloride m. 247-9.degree. (decompn.)]; N-benzyl-N'-(cafein-8-  
yl)ethylenediamine, --, --, 228-30.degree.; N,N-dibenzyl-N'-(cafein-8-  
yl)ethylenediamine, --, --, 195-7.degree.; N-isoamyl-N'-(cafein-8-  
yl)ethylenediamine, --, --, 223-5.degree.; 1-piperidino-3-(cafein-8-  
yl)aminopropane, 173-5.degree., C6H6-petr. ether, --; 1-pyrrolidino-3-  
(cafein-8-yl)aminopropane, 165-7.degree., C6H6-Petr. ether, --;  
N-phenyl-N'-(cafein-8-yl)trimethyl-enediamine, 159-61.degree., EtOH, --;  
N-(cafein-8-yl)-N'-(1-methylphenethyl)trimethylenediamine, 163-5.degree.,  
EtOH, --; N-(cafein-8-yl)-N'-(1-hydroxyethyl)trimethylenediamine,  
175-7.degree., H2O, --; N-(cafein-8-yl)-N',N'-bis(2-  
hydroxyethyl)ethylenediamine, 142-4.degree., EtOH, --;  
8-(4-methylpiperazino)caffeine, 148-50.degree., PhMe-petr. ether,  
344-6.degree. (methobromide m. 315-17.degree.; methiodide m.  
314-16.degree.); salt between 8-hydroxycaffeine and N,N-  
diethyltrimethylenediamine, 226.degree., EtOH.

IT 33236-53-2, Caffeine, 8-[2-(diethylamino)ethyl]amino]-,  
hydrochloride 88893-64-5, Caffeine, 8-[3-  
(diethylamino)propyl]amino]- 88893-65-6, Caffeine,  
8-[3-(diethylamino)propyl]amino]-, methiodide 96635-35-7,  
Caffeine, 8-[2-[2-(hydroxyethyl)amino]propyl]-amino]- 96714-63-5  
, Caffeine, 8-[3-(dimethylamino)propyl]amino]- 96729-64-5,  
Caffeine, 8-[3-(dimethylamino)propyl]amino]-, hydrochloride  
97302-63-1, Caffeine, 8-[2-(diethylamino)ethyl]amino]-  
97302-64-2, Caffeine, 8-[2-[bis(2-hydroxyethyl)amino]ethyl]-  
amino]- 97405-86-2, Caffeine, 8-[2-(diethylamino)ethyl]amino]-,  
methobromide 97526-13-1, Caffeine, 8-[3-  
(diethylamino)propyl]amino]-, methobromide 97725-29-6, Caffeine,  
8-[3-(diethylamino)propyl]amino]-, hydrochloride 97725-30-9,  
Caffeine, 8-[2-(isopentylamino)ethyl]amino]-, hydrochloride  
98053-69-1, Caffeine, 8-[2-(benzylamino)ethyl]amino]-,  
hydrochloride 98146-24-8, Caffeine, 8-[3-anilinopropyl]amino]-  
98223-07-5, Caffeine, 8-[3-(cyclohexylamino)propyl]amino]-  
100150-05-8, Caffeine, 8-[3-[(alpha-  
methylphenethyl)amino]propyl]amino]- 101941-95-1, Caffeine,  
8-[2-(dibenzylamino)ethyl]amino]-, hydrochloride  
(prepn. of)

RN 33236-53-2 HCPLUS

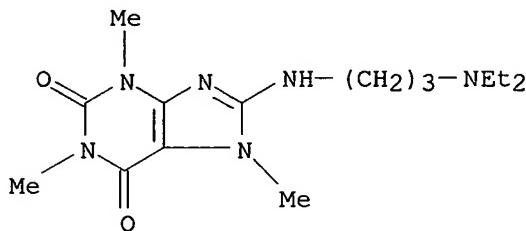
CN 1H-Purine-2,6-dione, 8-[2-(diethylamino)ethyl]amino]-3,7-dihydro-1,3,7-  
trimethyl-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 88893-64-5 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[3-(diethylamino)propyl]amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



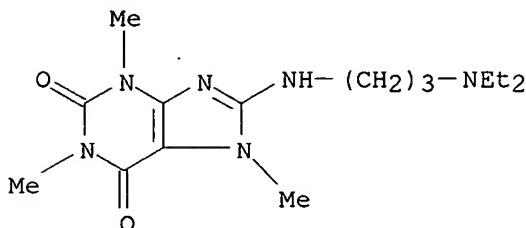
RN 88893-65-6 HCAPLUS

CN Caffeine, 8-[3-(diethylamino)propyl]amino-, methiodide (7CI) (CA INDEX NAME)

CM 1

CRN 88893-64-5

CMF C<sub>15</sub> H<sub>26</sub> N<sub>6</sub> O<sub>2</sub>



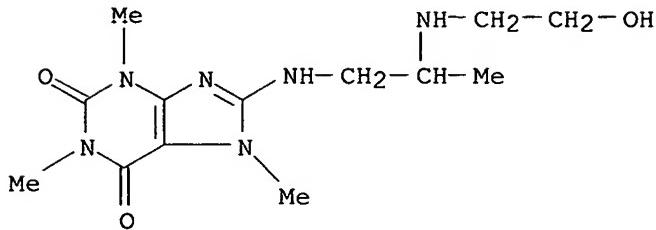
CM 2

CRN 74-88-4

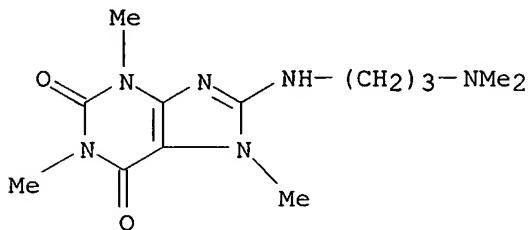
CMF C H<sub>3</sub> I

H<sub>3</sub>C-I

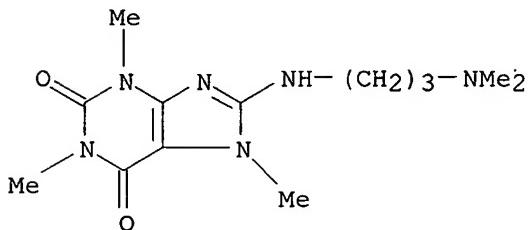
RN 96635-35-7 HCAPLUS  
CN Caffeine, 8-[{2-[{(2-hydroxyethyl)amino}propyl]amino}- (7CI) (CA INDEX NAME)



RN 96714-63-5 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[{3-(dimethylamino)propyl]amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

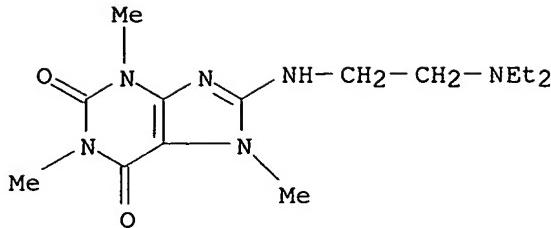


RN 96729-64-5 HCAPLUS  
CN Caffeine, 8-[{3-(dimethylamino)propyl]amino}-, hydrochloride (7CI) (CA INDEX NAME)

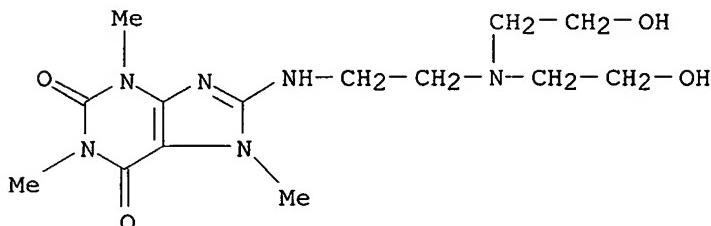


● HCl

RN 97302-63-1 HCAPLUS  
CN Caffeine, 8-[{2-(diethylamino)ethyl]amino}- (7CI) (CA INDEX NAME)



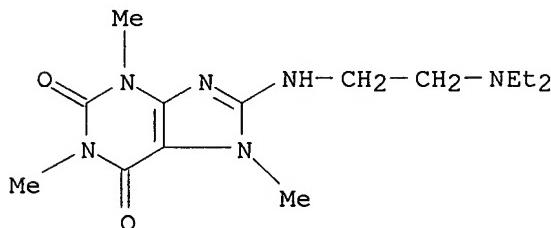
RN 97302-64-2 HCAPLUS  
 CN Caffeine, 8-[2-[bis(2-hydroxyethyl)amino]ethyl]amino-, (7CI) (CA INDEX NAME)



RN 97405-86-2 HCAPLUS  
 CN Caffeine, 8-[2-(diethylamino)ethyl]amino-, methobromide (7CI) (CA INDEX NAME)

CM 1

CRN 97302-63-1  
 CMF C14 H24 N6 O2



CM 2

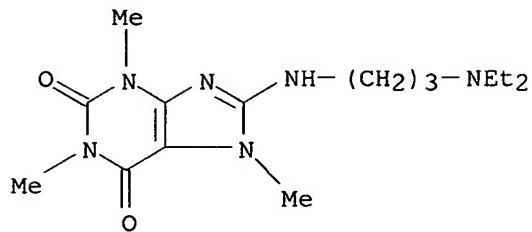
CRN 74-83-9  
 CMF C H3 Br

Br-CH<sub>3</sub>

RN 97526-13-1 HCAPLUS  
 CN Caffeine, 8-[3-(diethylamino)propyl]amino-, methobromide (7CI) (CA INDEX NAME)

CM 1

CRN 88893-64-5  
CMF C15 H26 N6 O2

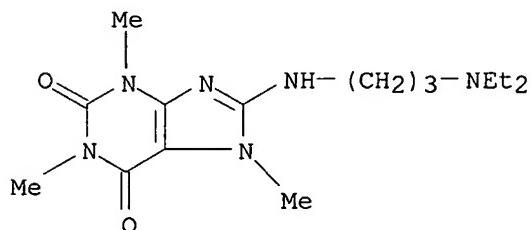


CM 2

CRN 74-83-9  
CMF C H3 Br

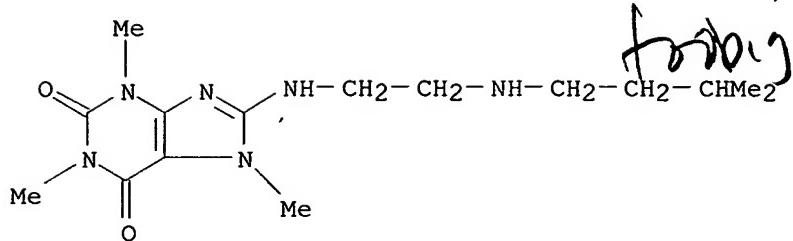
Br-CH3

RN 97725-29-6 HCAPLUS  
CN Caffeine, 8-[3-(diethylamino)propyl]amino-, hydrochloride (7CI) (CA INDEX NAME)



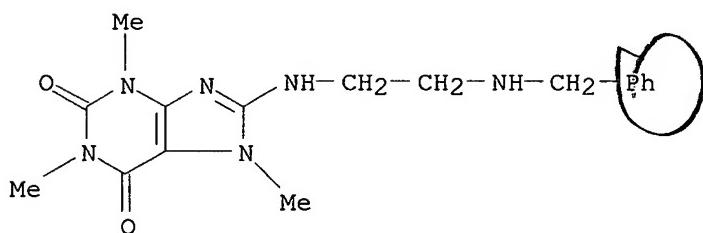
●x HCl

RN 97725-30-9 HCAPLUS  
CN Caffeine, 8-[2-(isopentylamino)ethyl]amino-, hydrochloride (7CI) (CA INDEX NAME)



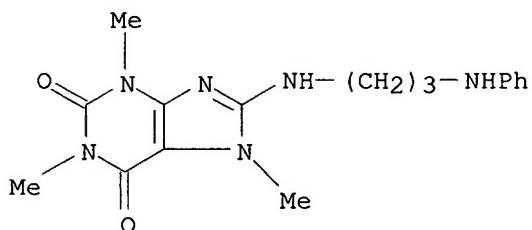
● x HCl

RN 98053-69-1 HCAPLUS  
CN Caffeine, 8-[(2-(benzylamino)ethyl]amino]-, hydrochloride (7CI) (CA INDEX NAME)

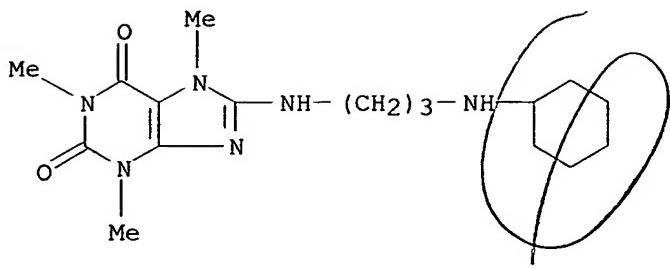


● x HCl

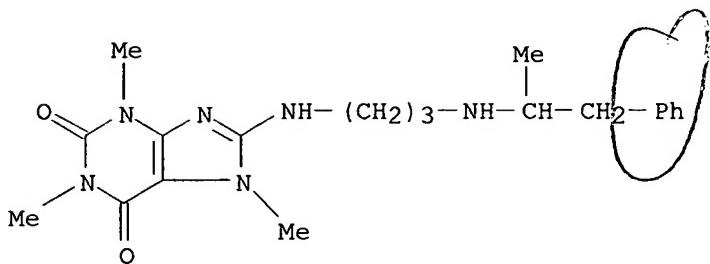
RN 98146-24-8 HCAPLUS  
CN Caffeine, 8-[(3-anilinopropyl)amino]- (7CI) (CA INDEX NAME)



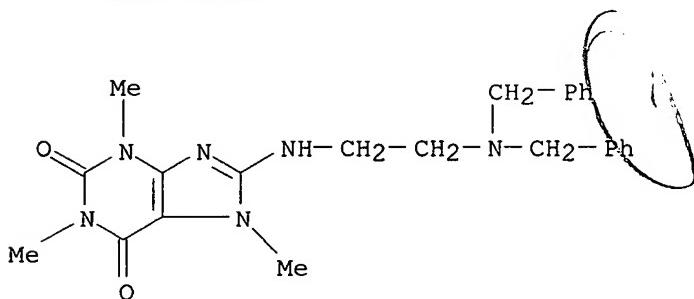
RN 98223-07-5 HCAPLUS  
CN Caffeine, 8-[(3-(cyclohexylamino)propyl]amino]- (7CI) (CA INDEX NAME)



RN 100150-05-8 HCAPLUS  
 CN Caffeine, 8-[3-[(alpha.-methylphenethyl)amino]propyl]amino]- (7CI) (CA INDEX NAME)

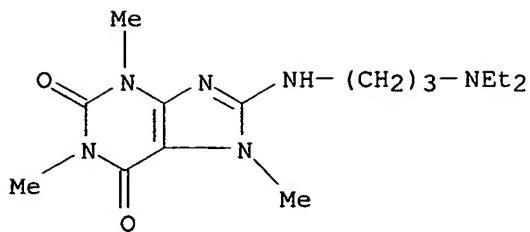


RN 101941-95-1 HCAPLUS  
 CN Caffeine, 8-[2-(dibenzylamino)ethyl]amino]-, hydrochloride (7CI) (CA INDEX NAME)

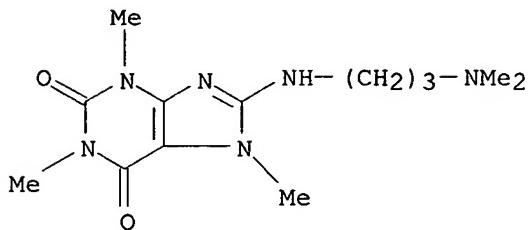


● x HCl

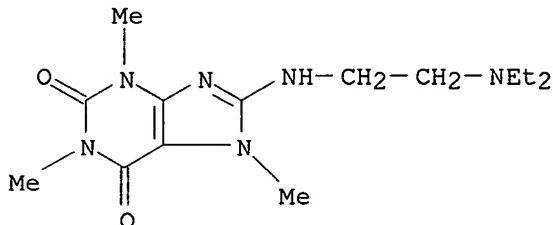
L23 ANSWER 36 OF 36 HCAPIUS COPYRIGHT 2002 ACS  
 1962:9246 Document No. 56:9246 Original Reference No. 56:1767a-b Action of some new 8-substituted derivatives of caffeine on vegetable cells.  
 Constantinescu, D. Gr.; Retezeanu, Marie; Constantinescu, Marguerite;  
 Stoenescu, V. Compt. Rend., 253, 176-8 (Unavailable) 1961.  
 AB Introduction of various chem. groups on position 8 of caffeine causes effects on the morphology of cells when treated with these derivs.  
 IT 88893-64-5, Caffeine, 8-[3-(diethylamino)propyl]amino]-  
 96714-63-5, Caffeine, 8-[3-(dimethylamino)propyl]amino]-  
 97302-63-1, Caffeine, 8-[2-(diethylamino)ethyl]amino]-  
 (plant-cell response to)  
 RN 88893-64-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[3-(diethylamino)propyl]amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 96714-63-5 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[3-(dimethylamino)propyl]amino]-3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 97302-63-1 HCPLUS  
 CN Caffeine, 8-[2-(diethylamino)ethyl]amino]- (7CI) (CA INDEX NAME)

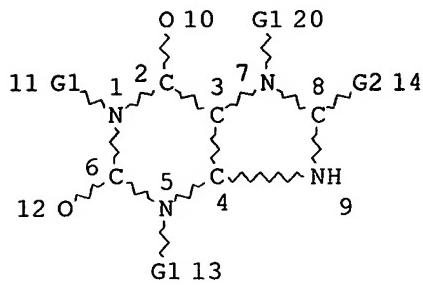


=> fil reg			
COST IN U.S. DOLLARS	SINCE FILE	TOTAL	
	ENTRY	SESSION	
FULL ESTIMATED COST	158.41	692.09	
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL	
	ENTRY	SESSION	
CA SUBSCRIBER PRICE	-22.30	-24.07	

FILE 'REGISTRY' ENTERED AT 13:58:51 ON 03 DEC 2002  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2002 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

```
=> d 14 que stat;fil hcap;s 14  
L1                 STR
```



```
N @15             G1~N~~C  
16 @17 19         C @18
```

VAR G1=H/C

VAR G2=15/17/18

NODE ATTRIBUTES:

```
NSPEC IS R AT 15  
NSPEC IS RC AT 18  
NSPEC IS RC AT 19  
CONNECT IS M1 RC AT 10  
CONNECT IS M1 RC AT 12  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED
```

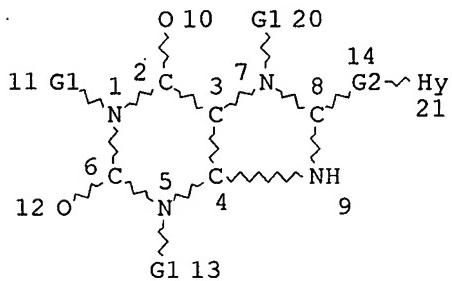
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE

```
L2             5409 SEA FILE=REGISTRY SSS FUL L1  
L3             STR
```



VAR G1=H/C

REP G2=(0-2) C

NODE ATTRIBUTES:

```
CONNECT IS M1 RC AT 10  
CONNECT IS M1 RC AT 12  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED
```

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

```
L4             481 SEA FILE=REGISTRY SUB=L2 SSS FUL L3
```

100.0% PROCESSED 5409 ITERATIONS

481 ANSWERS

SEARCH TIME: 00.00.01

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	34.19	34.40

FILE 'HCAPLUS' ENTERED AT 14:21:04 ON 03 DEC 2002  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 3 Dec 2002 VOL 137 ISS 23  
FILE LAST UPDATED: 2 Dec 2002 (20021202/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

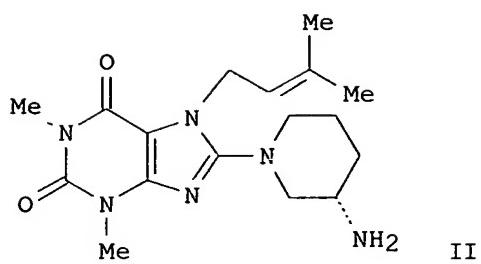
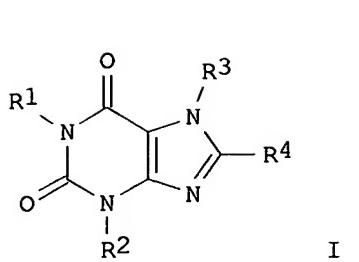
CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

L5 163 L4

=> d 1-163 cbib abs hitstr

L5 ANSWER 1 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
2002:676018 Document No. 137:216824 Preparation of xanthine derivatives as dipeptidylpeptidase-IV inhibitors. Himmelsbach, Frank; Mark, Michael; Eckhardt, Matthias; Langkopf, Elke; Maier, Roland; Lotz, Ralf (Boehringer Ingelheim Pharma K.-G., Germany). PCT Int. Appl. WO 2002068420 A1 20020906, 373 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2002-EP1820 20020221. PRIORITY: DE 2001-10109021 20010224; DE 2001-10117803 20010410; DE 2001-10140345 20010817; DE 2002-10203486 20020130.

GI



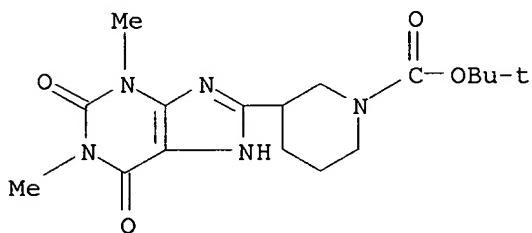
AB Xanthine derivs. of formula I [R1, R2 = H, alkyl, alkenyl, etc.; R3 = alkyl, arylalkyl, etc.; R4 = heterocyclyl, cycloalkyl, aminoalkyl, etc.] are prep'd. which exhibit an inhibitory effect on the activity of the dipeptidylpeptidase-IV enzyme. Pharmaceutical comps. contg. I are described. Thus, II was prep'd. and had an IC<sub>50</sub> of 22 nM against dipeptidylpeptidase-IV.

454710-05-5B

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of xanthine derivs. as dipeptidylpeptidase-IV inhibitors)

RN 454710-05-5 HCAPLUS

CN 1-Piperidinecarboxylic acid, 3-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 2 OF 163 HCPLUS COPYRIGHT 2002 ACS

2002:675841 Document No. 137:210952 Methods using xanthine glycol derivatives for treating irritable bowel syndrome and functional dyspepsia. Huber, Brian E.; Mangel, Allen Wayne (Smithkline Beecham Corporation, USA). PCT Int. Appl. WO 2002067942 A2 20020906, 54 pp.

DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ,  
 CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,  
 GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO,  
 RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ,  
 CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC,  
 ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.

APPLICATION: WO 2002-US5973 20020226. PRIORITY: US 2001-PV272115

AB 20010228.  
The invention discloses the use of glycol derivs. of xanthines for the treatment of irritable bowel syndrome and functional dyspepsia. The compds. of the invention are cell adhesion mol. inhibitors, preferably endothelial cell adhesion mol. inhibitors.

IT 259226-39-6 259226-40-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

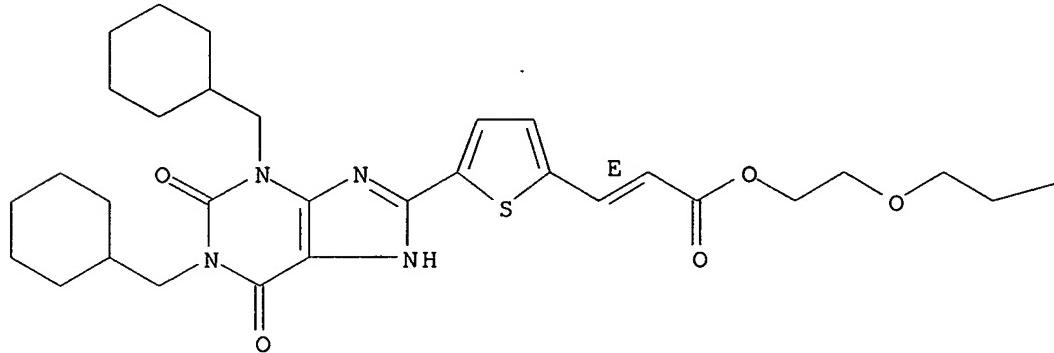
(xanthine glycol derivs. for treatment of irritable bowel syndrome and functional dyspepsia)

RN 259226-39-6 HCAPLUS

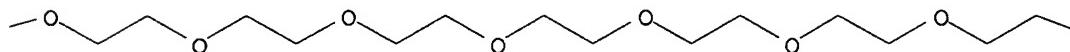
CN 2-Propenoic acid, 3-[5-[1,3-bis(cyclohexylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]-2-thienyl]-, 3,6,9,12,15,18,21,24,27-nonaoxaoctacos-1-yl ester, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



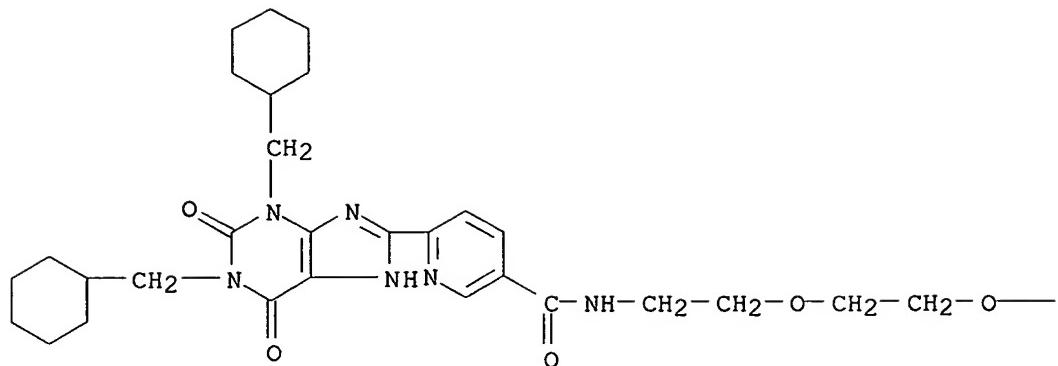
PAGE 1-C

OMe

RN 259226-40-9 HCAPLUS

CN 3-Pyridinecarboxamide, 6-[1,3-bis(cyclohexylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]-N-3,6,9,12,15,18,21,24,27-nonaoxaoctacos-1-yl- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

$\text{--CH}_2\text{CH}_2\text{O--CH}_2\text{CH}_2\text{O--CH}_2\text{CH}_2\text{O--CH}_2\text{CH}_2\text{O--CH}_2\text{CH}_2\text{O--}$

PAGE 1-C

$\text{--CH}_2\text{CH}_2\text{O--CH}_2\text{CH}_2\text{OMe}$

L5 ANSWER 3 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2002:556104 Document No. 137:109489 Compositions comprising a polypeptide and an active agent. Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal J. (USA). U.S. Pat. Appl. Publ. US 2002099013 A1 20020725, 34 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-933708 20010822. PRIORITY: US 2000-PV247928; 20001114; US 2000-PV247621; 20001114; US 2000-PV247620; 20001114; US 2000-PV247595; 20001114; US 2000-PV247594;

Searched by: Mary Hale 308-4258 CM-1 1E01

20001114; US 2000-PV247635; 20001114; US 2000-PV247634; 20001114; US 2000-PV247606; 20001114; US 2000-PV247607; 20001114; US 2000-PV247608; 20001114; US 2000-PV247609; 20001114; US 2000-PV247610; 20001114; US 2000-PV247611; 20001114; US 2000-PV247702; 20001114; US 2000-PV247701; 20001114; US 2000-PV247700; 20001114; US 2000-PV247699; 20001114; US 2000-PV247698; 20001114; US 2000-PV247807; 20001114; US 2000-PV247833; 20001114.

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the compn. to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prep'd. from Glu(OBut)NCA and cephalixin hydrochloride.

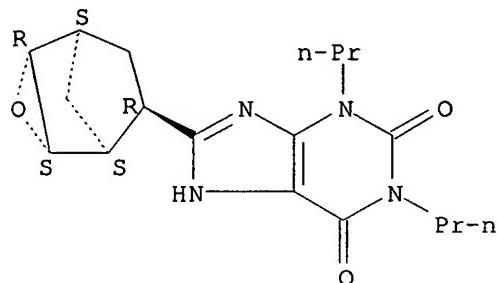
IT 166374-48-7, CVT 124

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(compns. comprising a polypeptide and an active agent)

RN 166374-48-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 4 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2002:332011 Document No. 136:355482 Compositions comprising a polypeptide and an active agent. Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randall J. (New River Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2002034237 A1 20020502, 98 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US26142 20010822. PRIORITY: US 2000-642820 20000822.

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the compn. to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prep'd. from Glu(OBut)NCA and cephalixin hydrochloride.

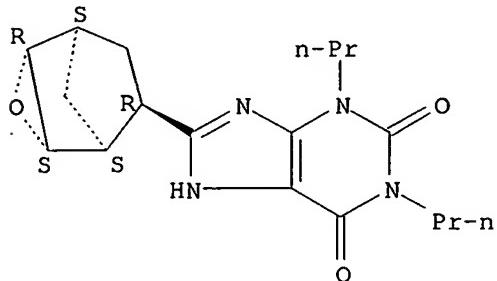
IT 166374-48-7, CVT 124

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(compns. comprising a polypeptide and an active agent)

RN 166374-48-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 5 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2002:312620 Document No. 137:272995 BG9719 (CVT-124), an A1 adenosine receptor antagonist, protects against the decline in renal function observed with diuretic therapy. Gottlieb, Stephen S.; Brater, D. Craig; Thomas, Ignatius; Havranek, Edward; Bourge, Robert; Goldman, Steven; Dyer, Farere; Gomez, Miguel; Bennett, Donald; Ticho, Barry; Beckman, Evan; Abraham, William T. (University of Maryland School of Medicine, D.V.A. Medical Center, Baltimore, MD, 21201, USA). Circulation, 105(11), 1348-1353 (English) 2002. CODEN: CIRCAZ. ISSN: 0009-7322. Publisher: Lippincott Williams & Wilkins.

AB Background-Adenosine may adversely affect renal function via its effects on renal arterioles and tubuloglomerular feedback, but effects of adenosine blockade in humans receiving furosemide and ACE inhibitors is unknown. Methods and Results-This was a randomized, double-blind, ascending-dose, crossover study evaluating 3 doses of BG9719 in 63 patients with congestive heart failure. Patients received placebo or 1 of 3 doses of BG9719 on 1 day and the same medication plus furosemide on a sep. day. Renal function and electrolyte and water excretion were assessed. BG9719 alone caused an increase in urine output and sodium excretion ( $P<0.05$ ). Although administration of furosemide alone caused a large diuresis, addn. of BG9719 to furosemide increased diuresis, which was significant at the 0.75-.mu.g/mL concn. BG9719 alone improved glomerular filtration rate (GFR) at the 2 lower doses. Furosemide alone caused a decline in GFR. When BG9719 was added to furosemide, however, creatinine clearance remained at baseline at the 2 lower doses. Conclusions-In patients with congestive heart failure on std. therapy, including ACE inhibitors, BG9719 increased both urine output and GFR. In these same patients, furosemide increased urine output at the expense of decreased GFR. When BG9719 was given in addn. to furosemide, urine vol. addnl. increased and there was no deterioration in GFR. A1 adenosine antagonism might preserve renal function while simultaneously promoting natriuresis during treatment for heart failure.

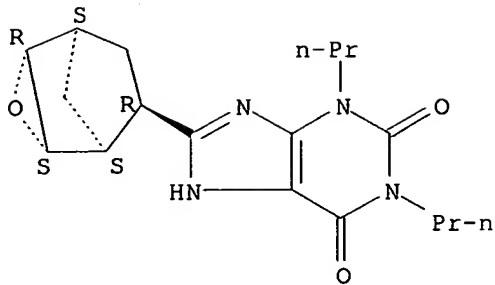
IT 166374-48-7, BG9719

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(BG9719 (CVT-124), A1 adenosine receptor antagonist, protects against decline in renal function obsd. with diuretic therapy)

RN 166374-48-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 6 OF 163 HCAPLUS COPYRIGHT 2002 ACS

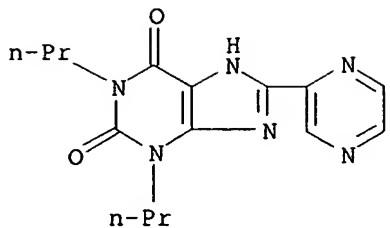
2002:308231 Document No. 137:56985 Structure-activity relationships at human and rat A2B adenosine receptors of xanthine derivatives substituted at the 1-, 3-, 7-, and 8-positions. Kim, Soon-Ai; Marshall, Melissa A.; Melman, Neli; Kim, Hak Sung; Mueller, Christa E.; Linden, Joel; Jacobson, Kenneth A. (Molecular Recognition Section Laboratory of Bioorganic Chemistry National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA). Journal of Medicinal Chemistry, 45(11), 2131-2138 (English) 2002. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 137:56985. Publisher: American Chemical Society.

AB In the search for improved selective antagonist ligands of the A2B adenosine receptor, which have the potential as antiasthmatic or antidiabetic drugs, we have synthesized and screened a variety of alkylxanthine derivs. substituted at the 1-, 3-, 7-, and 8-positions. Competition for <sup>125</sup>I-ABOPX (<sup>125</sup>I-3-(4-amino-3-iodobenzyl)-8-(phenyl-4-oxyacetate)-1-propylxanthine) binding in membranes of stably transfected HEK-293 cells revealed uniformly higher affinity (<10-fold) of these xanthines for human than for rat A2B adenosine receptors. Binding to rat brain membranes expressing A1 and A2A adenosine receptors revealed greater A2B selectivity over A2A than A1 receptors. Substitution at the 1-position with 2-phenylethyl (or alkyl/olefinic groups) and at N-3 with hydrogen or Me favored A2B selectivity. Relative to enprofylline, pentoxyfylline was equipotent and 1-propylxanthine was >13-fold more potent at human A2B receptors. Most N-7 substituents did not enhance affinity over hydrogen, except for 7-(2-chloroethyl), which enhanced the affinity of theophylline by 6.5-fold to 800 nM. The A2B receptor affinity-enhancing effects of 7-(2-chloroethyl) vs 7-Me were comparable to the known enhancement produced by an 8-aryl substitution. Among 8-Ph analogs, a larger alkyl group at the 1-position than at the 3-position favored affinity at the human A2B receptor, as indicated by 1-allyl-3-methyl-8-phenylxanthine, with a Ki value of 37 nM. Substitution on the 8-Ph ring indicated that an electron-rich ring was preferred for A2B receptor binding. In conclusion, new leads for the design of xanthines substituted in the 1-, 3-, 7-, and 8-positions as A2B receptor-selective antagonists have been identified.

IT 112683-71-3  
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)  
(structure-activity relationships at human and rat A2B adenosine receptors of xanthine derivs.)

RN 112683-71-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-pyrazinyl- (9CI) (CA INDEX NAME)



L5 ANSWER 7 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2001:915602 Document No. 136:303408 New developments in A1 and A2 adenosine receptor antagonists. Kiec-Kononowicz, K.; Drabczynska, A.; Pekala, E.; Michalak, B.; Miller, C. E.; Schumacher, B.; Karolak-Wojciechowska, J.; Duddeck, H.; Rockitt, S.; Wartchow, R. (IUPAC Commission, Medical College, Department of Chemical Technology of Drugs, Jagiellonian University, Krakow, PL 30-688, Pol.). Pure and Applied Chemistry, 73(9), 1411-1420 (English) 2001. CODEN: PACHAS. ISSN: 0033-4545. Publisher: International Union of Pure and Applied Chemistry.

AB A review with refs. The aim of this article is to briefly present progress in the development of the potent adenosine receptor (AR) antagonists with high selectivity for either A1, A2A or A2B ARs. The structural requirements for each AR subtype were discussed as well as their potential therapeutic use. In the search for new AR antagonists, series of imidazo-, pyrimido-, and diazepino-purindione derivs. as well as oxazolo-, oxazino-, and oxazepino-purindiones were designed, synthesized, and preliminarily evaluated in pharmacol. studies. Oxygen-contg. tricyclic derivs. were shown to be moderately potent AR antagonists exhibiting selectivity either for A1 or A2A ARs. Tricyclic purindiones with nitrogen in the third ring were generally more A2A AR selective. The compds. tested in vivo according to the Antiepileptic Drug Development Program of the National Institutes of Health (USA) were generally active as anticonvulsants in chem. induced seizures.

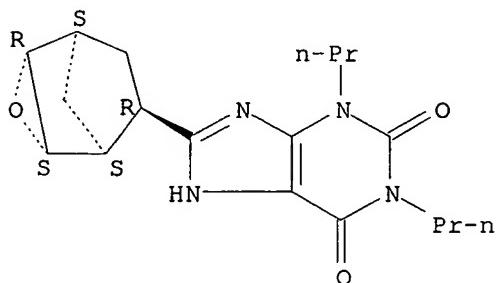
IT 166374-48-7P, Cvt 124

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(new developments in A1 and A2 adenosine receptor antagonists)

RN 166374-48-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 8 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2001:884756 Document No. 136:161106 A1 receptor blockade induces natriuresis with a favorable renal hemodynamic profile in SHHF/Mcc-facp rats

chronically treated with salt and furosemide. Jackson, Edwin K.; Kost, Curtis K., Jr.; Herzer, William A.; Smits, Glenn J.; Tofovic, Stevan P. (Center for Clinical Pharmacology, Departments of Pharmacology and Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA, USA). Journal of Pharmacology and Experimental Therapeutics, 299(3), 978-987 (English) 2001. CODEN: JPETAB. ISSN: 0022-3565. Publisher: American Society for Pharmacology and Experimental Therapeutics.

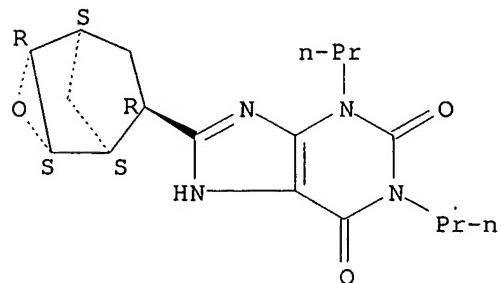
**AB**  
Our goal was to test the hypothesis that A1 receptor blockade induces diuresis/natriuresis with a favorable renal hemodynamic/cardiac profile in aged, lean SHHF/Mcc-facp rats, a rodent model of hypertensive dilated cardiomyopathy. Thirteen-month-old SHHF/Mcc-facp rats were pretreated for 72 h before expts. with furosemide (100 mg/kg by gavage 72, 48, and 24 h before expts.) to mimic the clin. setting of chronic diuretic therapy and were given 1% NaCl as drinking water to reduce dehydration/sodium depletion. Animals were instrumented for measurement of systemic and renal hemodynamics, renal excretory function, and cardiac performance, and baseline values were obtained during a 30-min clearance period. Animals then received either vehicle (n = 9), BG9719 [the S-enantiomer of 1,3-dipropyl-8-[2-(5,6-epoxynorbornyl)] xanthine (also called CVT-124)] (highly selective A1 receptor antagonist; 0.1 mg/kg bolus + 10 μg/kg/min; n = 9) or furosemide (loop diuretic; 30 mg/kg; n = 8) and measurements were repeated during four subsequent clearance periods. Both BG9719 and furosemide increased urine vol. and abs. and fractional sodium excretion. BG9719 increased renal blood flow and glomerular filtration rate, but did not affect fractional potassium excretion. Furosemide decreased renal blood flow and glomerular filtration rate and increased fractional potassium excretion. Neither drug altered afterload; however, furosemide, but not BG9719, decreased preload (central venous pressure and ventricular end diastolic pressure). Neither drug altered systolic function (+dP/dtmax); however, furosemide, but not BG9719, attenuated diastolic function (decreased -dP/dtmax, increased tau). In the setting of left ventricular dysfunction, chronic salt loading and prior loop diuretic treatment, selective A1 receptor antagonists are effective diuretic/natriuretic agents with a favorable renal hemodynamic/cardiac performance profile.

**IT**  
**166374-48-7, BG9719**  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(A1 receptor blockade induces natriuresis with a favorable renal hemodynamic/cardiac performance profile in SHHF/Mcc-facp rats chronically treated with salt and furosemide)

**RN** 166374-48-7 HCPLUS

**CN** 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 9 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2001:827599 Document No. 136:144648 Inhibition of human mast cell activation with the novel selective adenosine A2B receptor antagonist 3-isobutyl-8-pyrrolidinoxanthine (IPDX). Feoktistov, Igor; Garland, Emily M.; Goldstein, Anna E.; Zeng, Dewan; Belardinelli, Luiz; Wells, Jack N.; Biaggioni, Italo (Department of Medicine, Vanderbilt University, Nashville, TN, 37232, USA). Biochemical Pharmacology, 62(9), 1163-1173 (English) 2001. CODEN: BCPCA6. ISSN: 0006-2952. Publisher: Elsevier Science Inc..

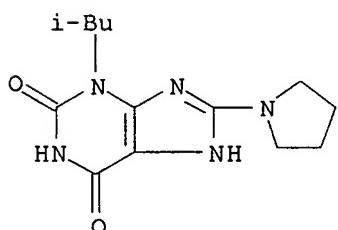
AB The antiasthmatic drug enprofylline was the first known selective, though not potent, A2B antagonist. On the basis of structure-activity relationships (SARs) of xanthine derivs., we designed a novel selective adenosine A2B receptor antagonist, 3-isobutyl-8-pyrrolidinoxanthine (IPDX), with potency greater than that of enprofylline. IPDX displaced [<sup>3</sup>H]ZM241385 ([<sup>3</sup>H]4-(2-[7-amino-2-(2-furyl)[1,2,4]triazolo[2,3-a]-[1,3,5]triazin-5-ylamino]ethyl)phenol) from human A2B adenosine receptors with a Ki value of 470.+-.2 nM and inhibited A2B-dependent cAMP accumulation in human erythroleukemia (HEL) cells with a KB value of 625.+-.71 nM. We found that IPDX was more selective than enprofylline toward human A2B receptors. It was 38-, 55-, and 82-fold more selective for human A2B than for human A1 (Ki value of 24.+-.8 .mu.M), human A2A (KB value of 36.+-.8 .mu.M), and human A3 (Ki value of 53.+-.10 .mu.M) adenosine receptors, resp. IPDX inhibited NECA (5'-N-ethylcarboxamidoadenosine)-induced interleukin-8 secretion in human mast cells (HMC-1) with a potency close to that detd. for A2B-mediated cAMP accumulation in HEL cells, thus confirming the role of A2B adenosine receptors in mediating human mast cell activation. Since adenosine triggers bronchoconstriction in asthmatic patients through human mast cell activation, IPDX may become a basis for the development of new antiasthmatic drugs with improved properties compared with those of enprofylline. Our data demonstrate that IPDX can be used as a tool to differentiate between A2B and other adenosine receptor-mediated responses.

IT 329024-77-3

RL: BUU (Biological use, unclassified); PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study); USES (Uses)  
(inhibition of human mast cell activation with novel selective adenosine A2B receptor antagonist 3-isobutyl-8-pyrrolidinoxanthine (IPDX))

RN 329024-77-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-(2-methylpropyl)-8-(1-pyrrolidinyl)-(9CI) (CA INDEX NAME)



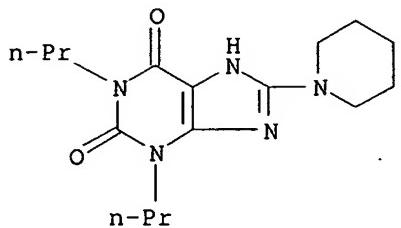
IT 108653-57-2 108653-58-3 108653-59-4

127946-21-8 132940-32-0

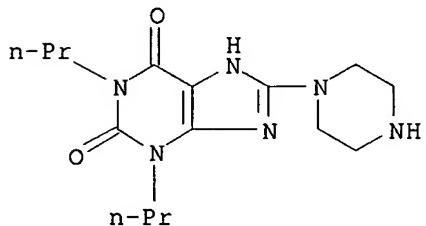
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)  
(structure activity relationship of xanthine derivs. as A2B adenosine receptor antagonists)

RN 108653-57-2 HCAPLUS

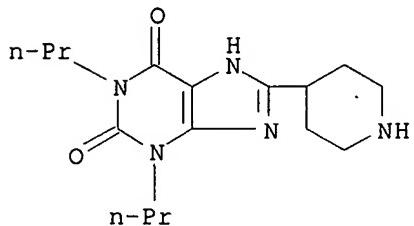
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



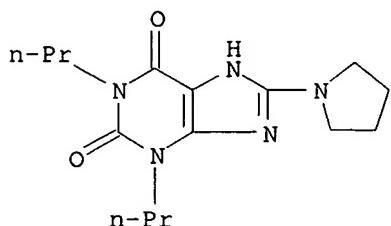
RN 108653-58-3 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-piperazinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



RN 108653-59-4 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)

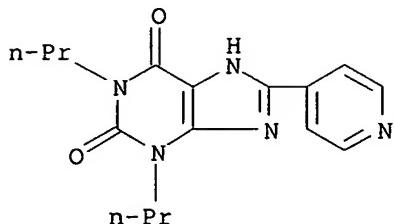


RN 127946-21-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(1-pyrrolidinyl)- (9CI)  
(CA INDEX NAME)



RN 132940-32-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 10 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2001:824514 Document No. 137:41460 Novel effects of selective adenosine subtype 1 (AI) receptor inhibition on renal and pulmonary function in heart failure. Lucas, David G., Jr.; Hendrick, Jennifer W.; Sample, Jeffrey A.; Dowdy, Kathryn B.; Escobar, Gladys P.; Crawford, Fred A., Jr.; Spinale, Francis G. (Division of Cardiothoracic Surgery, Medical University of South Carolina, Charleston, SC, USA). Surgical Forum, 52, 95-97 (English) 2001. CODEN: SUFOAX. ISSN: 0071-8041. Publisher: American College of Surgeons.

AB The acute effects of selective AI block were examd. in a model of heart failure (HF). HF was induced in pigs by chronic pacing, which reduced LV fractional shortening. Cardiac output decreased with HF compared with normal. Pulmonary capillary wedge pressure, pulmonary vascular resistance, and plasma renin activity were increased with HF compared with ref. control. Cardiac output remained unchanged between the AI block and vehicle groups throughout the study. Increased AI receptor activation contributes to renal-mediated fluid retention in HF. Selective AI blockade could induce a considerable diuresis without hemodynamic compromise in a model of HF. AI receptor blockade caused considerable diuresis in patients with HF, indicating that adenosine is a significant determinant of renal function in HF. Selective AI blockade may be a useful adjunctive diuretic in the setting of HF.

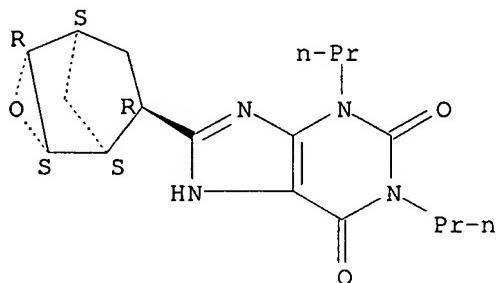
IT 166374-48-7, BG9719

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(novel effects of selective adenosine subtype 1 (AI) receptor inhibition with BG9719 on renal and pulmonary function in heart failure)

RN 166374-48-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

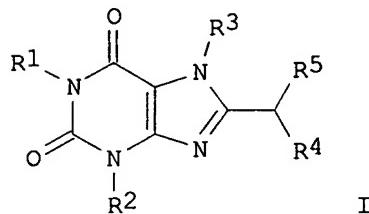
Absolute stereochemistry. Rotation (+).



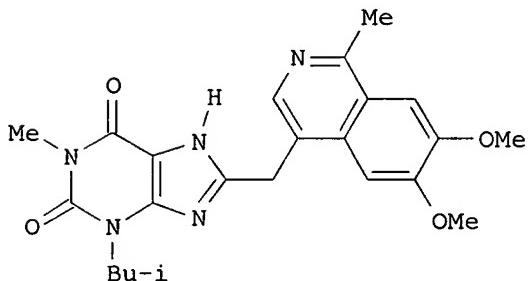
L5 ANSWER 11 OF 163 HCPLUS COPYRIGHT 2002 ACS

2001:762998 Document No. 135:303908 8-(Quinolinylmethyl)xanthine and  
8-(isoquinolinylmethyl)xanthine derivatives as PDE 5 inhibitors, useful  
for treatment of erectile dysfunction. Bhalay, Gurdip; Collingwood,  
Stephen Paul; Fairhurst, Robin Alec; Gomez, Sylvie Felicite; Naef, Reto;  
Sandham, David Andrew (Novartis A.-G., Switz.; Novartis-Erfindungen  
Verwaltungsgesellschaft m.b.H.). PCT Int. Appl. WO 2001077110 A1  
20011018, 70 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,  
BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES,  
FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,  
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,  
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ,  
CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC,  
ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.  
APPLICATION: WO 2001-EP3909 20010405. PRIORITY: GB 2000-8694 20000407.

GI



I



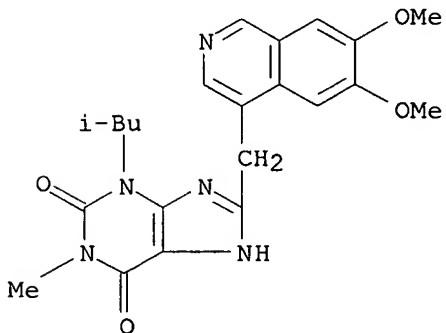
II

AB Compds. of formula I, in free or salt form, are disclosed [where R1 = H or alkyl (un)substituted by OH, alkoxy, or alkylthio; R2 = H, alkyl, hydroxyalkyl, alkylcarbonyloxyalkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, cycloalkylalkyl, heterocyclylalkyl, aralkyl [aryl ring optionally fused to 5-membered heterocyclic group or substituted by alkoxy, (di)(alkyl)amino, acylamino, halo, OH, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, alkylsulfonylamino or dialkylaminosulfonylamino]; R3 = H or alkyl optionally substituted by OH, alkoxy, or alkylthio; R4 = H or alkyl; R5 = (un)substituted quinolinyl, isoquinolinyl, or oxodihydroisoquinolinyl, optionally fused to 5-membered heterocyclic group [substituents = halo, cyano, OH, alkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkoxy, alkylthio, alkenyl, alkoxycarbonyl, alkynyl, carboxyl, acyl, N(R6)R7, (un)substituted aryl (substituents = halo or alkoxy), or 5- or 6-membered heteroaryl attached through ring C]; R6, R7 = H or alkyl (optionally substituted by OH or alkoxy); or 1 of R6 and R7 =

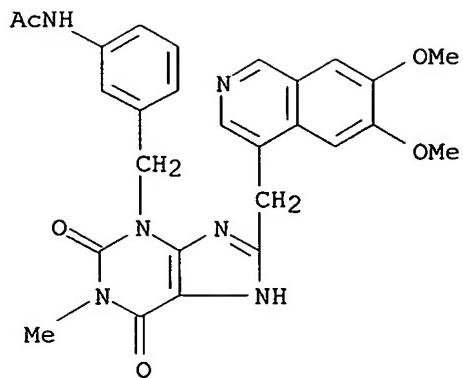
H, the other = acyl; or NR6R7 = 5- or 6- membered heterocyclyl]. I are inhibitors of cGMP phosphodiesterases (PDEs), and in particular are selective inhibitors of PDE5. They exhibit good selectivity for PDE5 over PDE1 and PDE6, indicating a low side-effect profile. I are of particular interest for use in the treatment of sexual dysfunction, esp. male erectile dysfunction. Examples include 87 product syntheses and 59 intermediate preps. Ten compds. are particularly preferred, and these are specifically claimed. For instance, cyclocondensation of 5,6-diamino-1-isobutyl-3-methyl-1H-pyrimidine-2,4-dione with (6,7-dimethoxy-1-methylisoquinolin-4-yl)acetic acid (preps. given), using EDC in aq. MeOH, gave the preferred title compd. II. In an in vitro assay for PDE5 inhibition, I gave IC<sub>50</sub> values of 0.0005 .mu.M to 10 .mu.M, e.g., 0.007 .mu.M for II.

IT 366444-48-6P, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihdropurine-2,6-dione 366444-49-7P, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-[3-(acetylamino)phenyl]methyl]-1-methyl-3,7-dihdropurine-2,6-dione 366444-51-1P, 3-Allyl-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihdropurine-2,6-dione hydrochloride salt 366444-56-6P, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3-(2-methylallyl)-3,7-dihdropurine-2,6-dione 366444-62-4P, 8-(7-Methoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihdropurine-2,6-dione 366444-91-9P, 8-(6-Bromoisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihdropurine-2,6-dione 366444-96-4P, 3-(3-Aminobenzyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihdropurine-2,6-dione 366445-02-5P, 8-(6,7-Dihydroxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihdropurine-2,6-dione 366445-06-9P, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(3-hydroxy-2-methylpropyl)-1-methyl-3,7-dihdropurine-2,6-dione  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(drug candidate; prepn. of quinoline-xanthine and isoquinoline-xanthine derivs. as PDE 5 inhibitors)

RN 366444-48-6 HCPLUS  
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

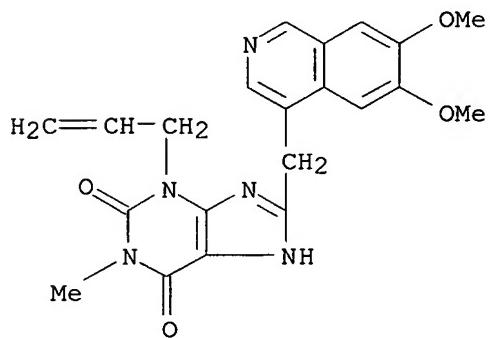


RN 366444-49-7 HCPLUS  
CN Acetamide, N-[3-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 366444-51-1 HCPLUS

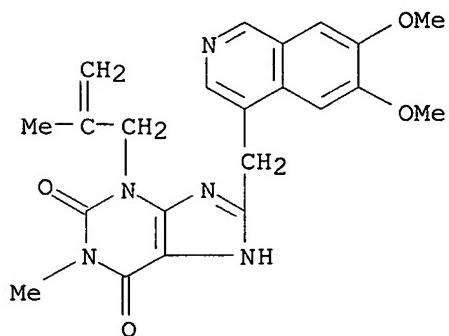
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-propenyl)-, hydrochloride (9CI) (CA INDEX NAME)



● x HCl

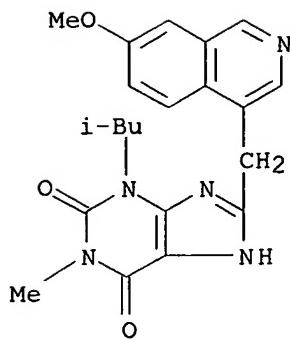
RN 366444-56-6 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methyl-2-propenyl)- (9CI) (CA INDEX NAME)

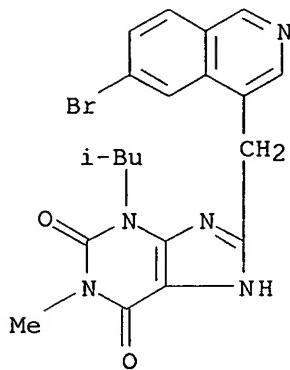


RN 366444-62-4 HCPLUS

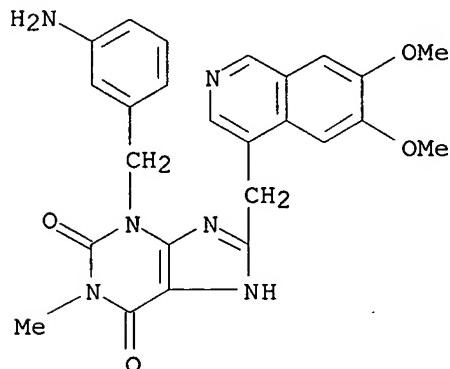
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(7-methoxy-4-isoquinolinyl)methyl]-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



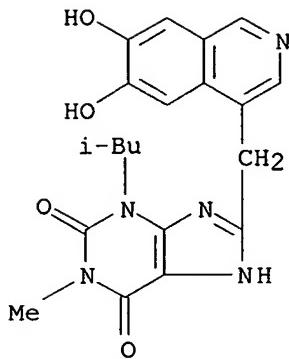
RN 366444-91-9 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(6-bromo-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366444-96-4 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3-[(3-aminophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

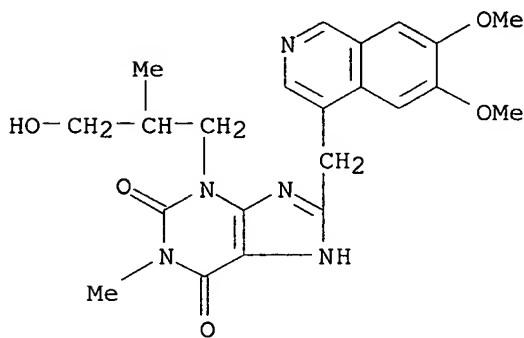


RN 366445-02-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(6,7-dihydroxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366445-06-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isquinolinyl)methyl]-3,7-dihydro-3-(3-hydroxy-2-methylpropyl)-1-methyl- (9CI) (CA INDEX NAME)

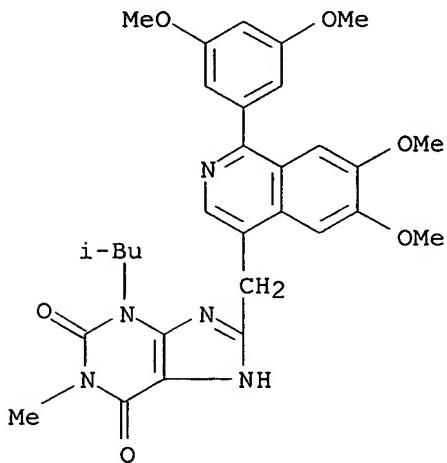


IT 366444-39-5P, 8-[6,7-Dimethoxy-1-(3,5-dimethoxyphenyl)isoquinolin-4-ylmethyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione  
 366444-40-8P, 8-[6,7-Dimethoxy-1-(3,5-diisopropoxyphenyl)isoquinolin-4-ylmethyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione 366444-41-9P, 8-[6-Isopropoxy-7-methoxy-1-(3,5-diisopropoxyphenyl)isoquinolin-4-ylmethyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione 366444-42-0P, 8-[6-Isopropoxy-7-methoxy-1-(3,5-dimethoxyphenyl)isoquinolin-4-ylmethyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione 366444-43-1P, 8-[(6-Isopropoxy-7-methoxy-1-tert-butylisoquinolin-4-yl)methyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione 366444-44-2P, 8-[(6-Isopropoxy-7-methoxy-1-isopropylisoquinolin-4-yl)methyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione 366444-45-3P, 8-(6,7-Dimethoxy-1-methylisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione 366444-46-4P, 8-[(6,7-Dimethoxy-1-tert-butylisoquinolin-4-yl)methyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione 366444-47-5P, 8-[(6,7-Dimethoxy-1-isopropylisoquinolin-4-yl)methyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione 366444-50-0P, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-methyl-3,7-dihydropurine-2,6-dione 366444-52-2P, 3-(Cyclopropylmethyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione 366444-53-3P, 3-Neopentyl-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione 366444-54-4P, 1,3-Diisobutyl-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-3,7-dihydropurine-2,6-dione 366444-55-5P, 3-(Cyclohexylmethyl)-8-(6,7-

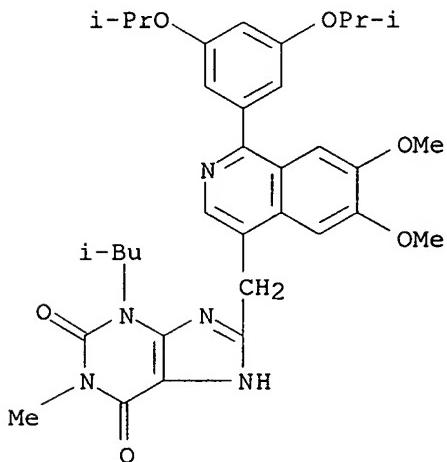
dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-57-7P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3-  
(tetrahydrofurfuryl)-3,7-dihydropurine-2,6-dione **366444-58-8P**,  
(S)-8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3-(2-methylbutyl)-3,7-  
dihydropurine-2,6-dione **366444-59-9P**, 3-Propyl-8-(6,7-  
dimethoxyisoquinolin-4-ylmethyl)-3,7-dihydropurine-2,6-dione  
**366444-60-2P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-[4-  
(acetylamino)phenyl]methyl]-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-61-3P**, 8-[(6,7-Methylenedioxyisoquinolin-4-yl)methyl]-3-  
isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366444-63-5P**,  
8-[1-(1-Chloro-7-methoxyisoquinolin-4-yl)ethyl]-3-isobutyl-1-methyl-3,7-  
dihydropurine-2,6-dione **366444-64-6P**, 8-[1-(1-Cyano-7-  
methoxyisoquinolin-4-yl)ethyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-  
dione **366444-65-7P**, 8-[1-(1-Morpholino-7-methoxyisoquinolin-4-  
yl)ethyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-66-8P**, 8-[(7-Hydroxy-6-methoxyisoquinolin-4-yl)methyl]-3-  
isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366444-67-9P**,  
8-(6,7-Dimethoxy-3-methylisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-  
dihydropurine-2,6-dione **366444-68-0P**, 8-(6,7-  
Dimethoxyisoquinolin-4-ylmethyl)-3-hexyl-1-methyl-3,7-dihydropurine-2,6-  
dione **366444-69-1P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-  
(3,4-dimethoxybenzyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-70-4P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(3,4-  
methylenedioxybenzyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-71-5P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(2,4-  
dichlorobenzyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-72-6P**  
, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(4-methoxybenzyl)-1-methyl-3,7-  
dihydropurine-2,6-dione **366444-73-7P**, 8-(1-Chloro-6,7-  
dimethoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-  
dione **366444-74-8P**, 8-(Isoquinolin-4-ylmethyl)-3-isobutyl-1-  
methyl-3,7-dihydropurine-2,6-dione **366444-75-9P**,  
8-(6-Ethoxy-7-methoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-  
dihydropurine-2,6-dione **366444-76-0P**, 8-(6,7-Dimethoxy-1-  
morpholinoisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-  
2,6-dione **366444-77-1P**, 8-[(6,7-Dimethoxy-1-(4-methyl-1-  
piperazinyl)isoquinolin-4-yl)methyl]-3-isobutyl-1-methyl-3,7-dihydropurine-  
2,6-dione **366444-78-2P**, 8-(7-Ethoxy-6-methoxyisoquinolin-4-  
ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-79-3P** **366444-80-6P** **366444-81-7P**,  
8-[(6,7-Dimethoxyisoquinolin-4-yl)ethyl]-3-isobutyl-1-methyl-3,7-  
dihydropurine-2,6-dione **366444-83-9P**, 3-Isobutyl-8-(6-  
methoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-84-0P**, (S)-8-(6-Methoxyisoquinolin-4-ylmethyl)-1-methyl-3-  
(2-methylbutyl)-3,7-dihydropurine-2,6-dione **366444-85-1P**,  
8-(6-Chloroisoquinolin-4-ylmethyl)-3-neopentyl-1-methyl-3,7-dihydropurine-  
2,6-dione **366444-86-2P**, 8-(6-Chloroisoquinolin-4-ylmethyl)-3-  
isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366444-87-3P**,  
8-(6-Methoxyisoquinolin-4-ylmethyl)-3-(cyclopropylmethyl)-1-methyl-3,7-  
dihydropurine-2,6-dione **366444-88-4P**, 8-(6-Chloroisoquinolin-4-  
ylmethyl)-3-(cyclopropylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-89-5P**, 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-  
(cyclobutylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-90-8P**, 8-(6-Methoxyisoquinolin-4-ylmethyl)-3-(2-  
methylallyl)-1-methyl-3,7-dihydropurine-2,6-dione **366444-92-0P**,  
8-(6-Methoxyisoquinolin-4-ylmethyl)-3-neopentyl-1-methyl-3,7-dihydropurine-  
2,6-dione **366444-93-1P**, 8-(6-Ethynylisoquinolin-4-ylmethyl)-3-  
isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366444-94-2P**,  
8-(8-Fluoro-6-methoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-  
dihydropurine-2,6-dione **366444-95-3P**, 8-(5-Bromo-6-  
methoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-

dione **366444-97-5P**, 3-[3-[(N,N-Dimethylsulfamoyl)amino]benzyl]-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-98-6P**, 3-[4-[(N,N-Dimethylsulfamoyl)amino]benzyl]-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366444-99-7P**, 3-[4-[(1-Methylethyl)sulfonyl]amino]benzyl]-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366445-00-3P**, 3-(4-Aminobenzyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-01-4P**,  
 8-(7-Hydroxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-03-6P**, 8-(8-Bromo-6,7-dihydroxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione  
**366445-04-7P**, 8-(8-Bromo-7-hydroxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-05-8P**,  
 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-3-(3-hydroxypropyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-07-0P**, Acetic acid  
 3-[8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-2,6-dioxo-1,2,6,7-tetrahydropurin-3-yl]-2-methylpropyl ester **366445-08-1P**,  
 8-(6,7-Dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3-[(1-methylcyclopropyl)methyl]-3,7-dihydropurine-2,6-dione **366445-09-2P**  
 , 8-(6-Methoxyisoquinolin-4-ylmethyl)-3-(cyclohexylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-10-5P**, 8-(6-Methoxyisoquinolin-4-ylmethyl)-3-(tetrahydrofuryl)-1-methyl-3,7-dihydropurine-2,6-dione  
**366445-11-6P**, 8-(7-Fluoro-6-methoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-12-7P**,  
 8-(6-Carboxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-13-8P**, 8-(5-Chloro-6-methoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione  
**366445-14-9P**, 4-[(3-Isobutyl-1-methyl-2,6-dioxo-2,3,6,7-tetrahydro-1H-purin-8-yl)methyl]isoquinoline-6-carbonitrile **366445-15-0P**,  
 8-(6-Ethylisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-16-1P**, 8-(6-Ethoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-17-2P**,  
 3-(4-Aminobenzyl)-8-(6-methoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-18-3P**, 3-[4-[(1-Methylethyl)sulfonyl]amino]benzyl]-8-(6-methoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-19-4P**,  
 3-[4-[(N,N-Dimethylamino)sulfonyl]amino]benzyl]-8-(6-methoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione **366445-20-7P**,  
 8-[1-(Dimethylamino)-6,7-dimethoxyisoquinolin-4-ylmethyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-21-8P**,  
 8-[6,7-Dimethoxy-1-(piperidin-1-yl)isoquinolin-4-ylmethyl]-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-22-9P**,  
 8-(1-Methyl-6-isopropoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-23-0P**, 8-(1-Methyl-6-ethoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-24-1P**, 3-Isobutyl-1-methyl-8-[1-(6-methyl-5-oxo-5,6-dihydro-1,3-dioxolo[4,5-g]isoquinolin-8-yl)ethyl]-3,7-dihydropurine-2,6-dione **366445-25-2P**, 8-(6,7-Dimethoxyquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366445-26-3P**,  
 8-(1-Methyl-6-methoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione **366446-17-5P**, 8-(1-Chloro-6,7-dimethoxyisoquinolin-4-ylmethyl)-3-isobutyl-1-methyl-3,7-dihydropurine-2,6-dione hydrochloride **366446-18-6P**, 3-(3-Aminobenzyl)-8-(6,7-dimethoxyisoquinolin-4-ylmethyl)-1-methyl-3,7-dihydropurine-2,6-dione dihydrochloride  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (drug candidate; prepn. of quinoline-xanthine and isoquinoline-xanthine derivs. as PDE 5 inhibitors)

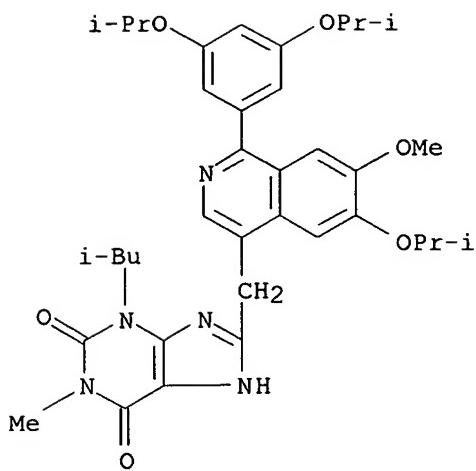
RN 366444-39-5 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[[1-(3,5-dimethoxyphenyl)-6,7-dimethoxy-4-isoquinolinyl]methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366444-40-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[[1-[3,5-bis(1-methylethoxy)phenyl]-6,7-dimethoxy-4-isoquinolinyl]methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

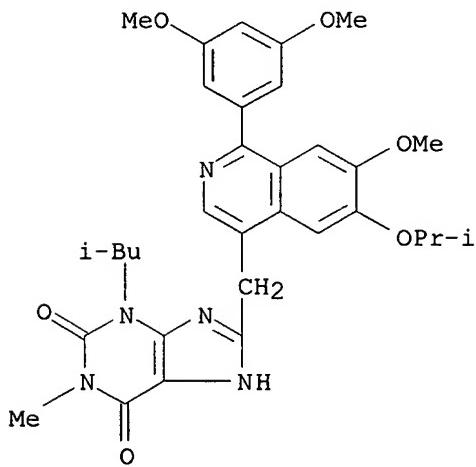


RN 366444-41-9 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[[1-[3,5-bis(1-methylethoxy)phenyl]-7-methoxy-6-(1-methylethoxy)-4-isoquinolinyl]methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



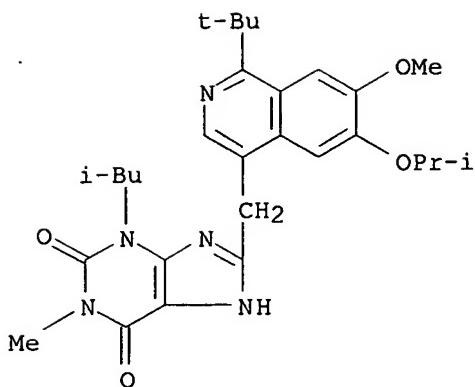
RN 366444-42-0 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1-(3,5-dimethoxyphenyl)-7-methoxy-6-(1-methylethoxy)-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



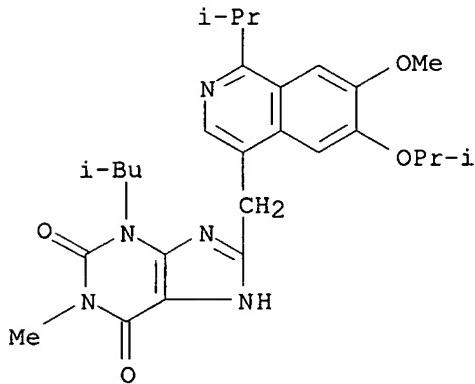
RN 366444-43-1 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(1-(1,1-dimethylethyl)-7-methoxy-6-(1-methylethoxy)-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



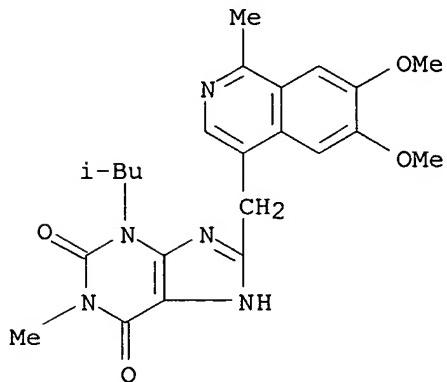
RN 366444-44-2 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[[7-methoxy-6-(1-methylethoxy)-1-(1-methylethyl)-4-isoquinolinyl]methyl]-1-methyl-3-(2-methylpropyl)- (9CI)  
(CA INDEX NAME)



RN 366444-45-3 HCPLUS

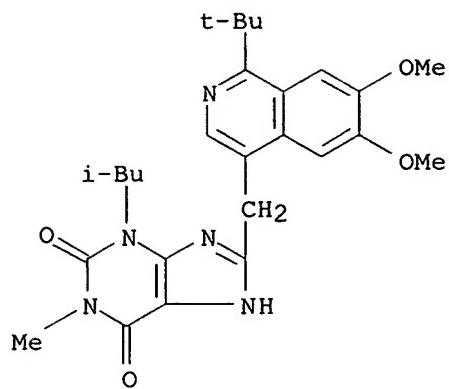
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-1-methyl-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366444-46-4 HCPLUS

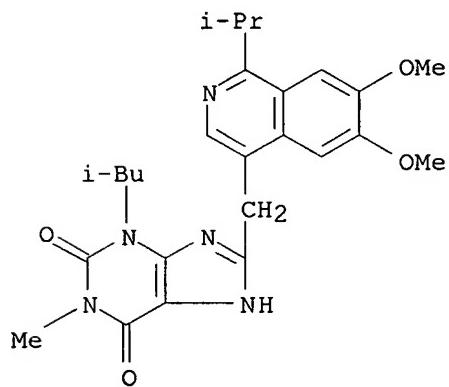
CN 1H-Purine-2,6-dione, 8-[[1-(1,1-dimethylethyl)-6,7-dimethoxy-4-isoquinolinyl]methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

INDEX NAME)



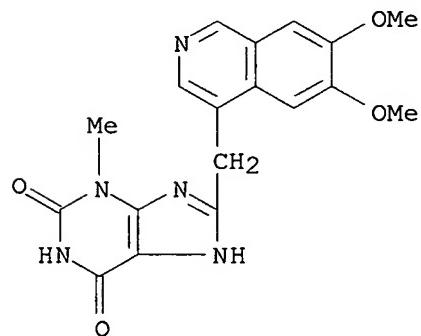
RN 366444-47-5 HCPLUS

CN 1H-Purine-2,6-dione, 8-[[6,7-dimethoxy-1-(1-methylethyl)-4-isoquinolinyl]methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366444-50-0 HCPLUS

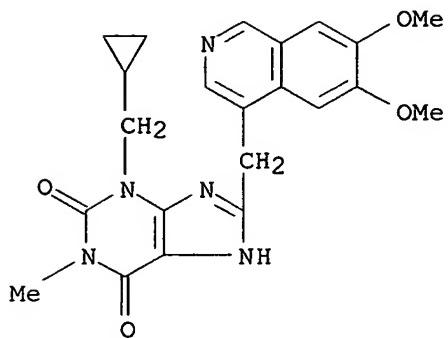
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-3-methyl- (9CI) (CA INDEX NAME)



RN 366444-52-2 HCPLUS

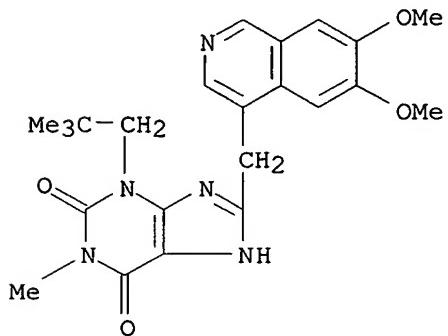
CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-8-[(6,7-dimethoxy-4-

isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



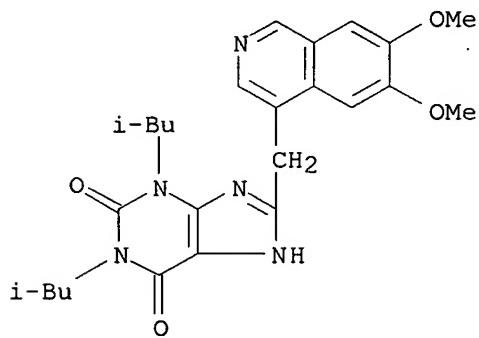
RN 366444-53-3 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3-(2,2-dimethylpropyl)-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



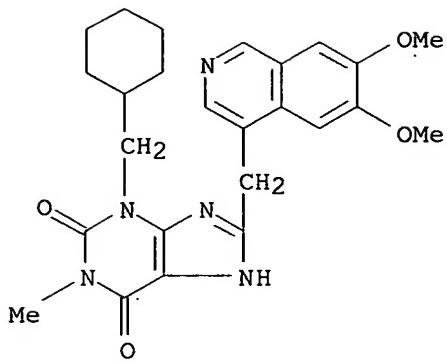
RN 366444-54-4 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1,3-bis(2-methylpropyl)- (9CI) (CA INDEX NAME)



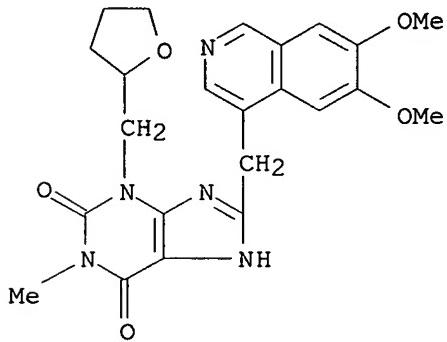
RN 366444-55-5 HCPLUS

CN 1H-Purine-2,6-dione, 3-(cyclohexylmethyl)-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 366444-57-7 HCAPLUS

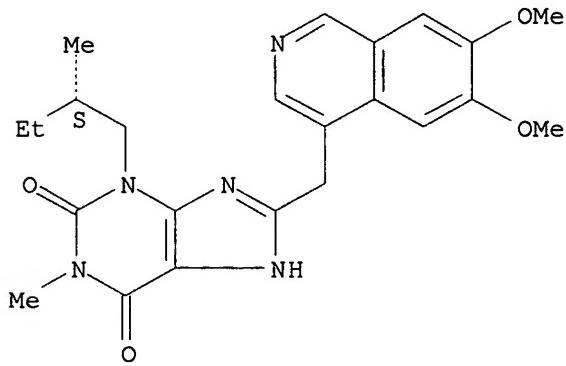
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isquinolinyl)methyl]-3,7-dihydro-1-methyl-3-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



RN 366444-58-8 HCAPLUS

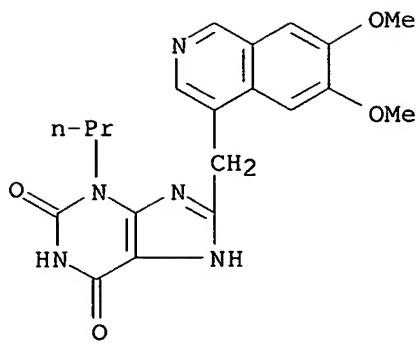
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isquinolinyl)methyl]-3,7-dihydro-1-methyl-3-[(2S)-2-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

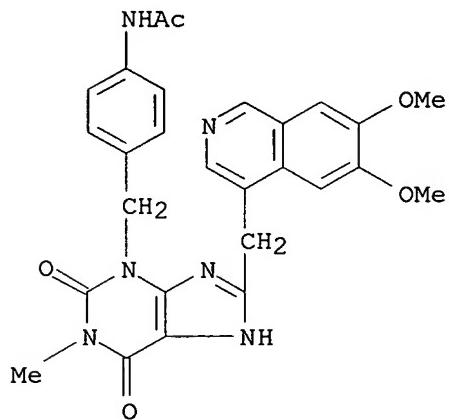


RN 366444-59-9 HCAPLUS

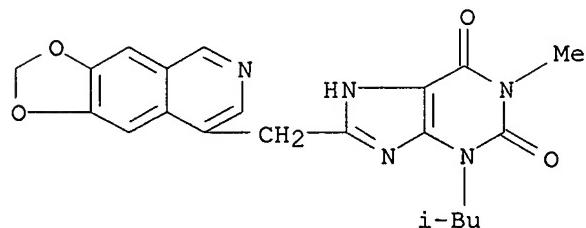
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isquinolinyl)methyl]-3,7-dihydro-3-propyl- (9CI) (CA INDEX NAME)



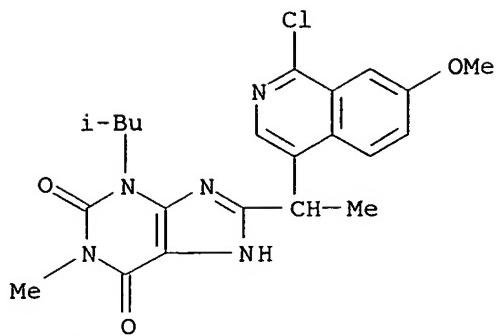
RN 366444-60-2 HCAPLUS  
 CN Acetamide, N-[4-[(8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl)methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 366444-61-3 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-(1,3-dioxolo[4,5-g]isoquinolin-8-ylmethyl)-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

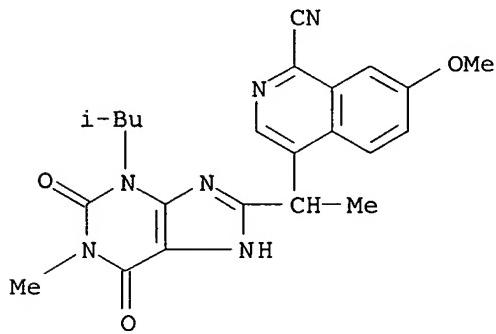


RN 366444-63-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[1-(1-chloro-7-methoxy-4-isoquinolinyl)ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



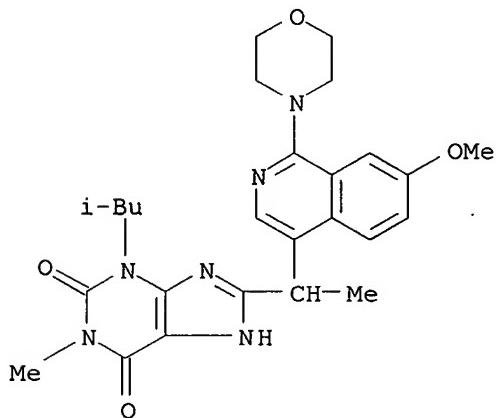
RN 366444-64-6 HCPLUS

CN 1-Isoquinolinecarbonitrile, 7-methoxy-4-[1-[2,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-2,6-dioxo-1H-purin-8-yl]ethyl]- (9CI) (CA INDEX NAME)



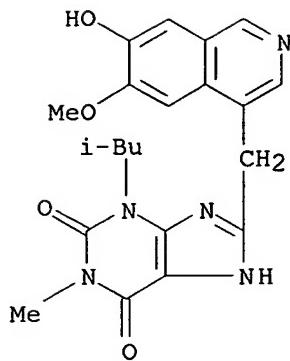
RN 366444-65-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[1-[7-methoxy-1-(4-morpholinyl)-4-isooquinolinyl]ethyl]-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



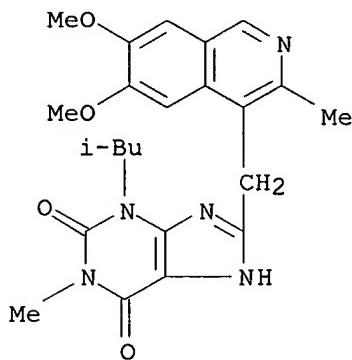
RN 366444-66-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(7-hydroxy-6-methoxy-4-isooquinolinyl)methyl]-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



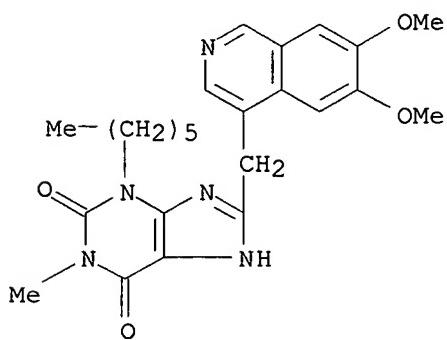
RN 366444-67-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-3-methyl-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



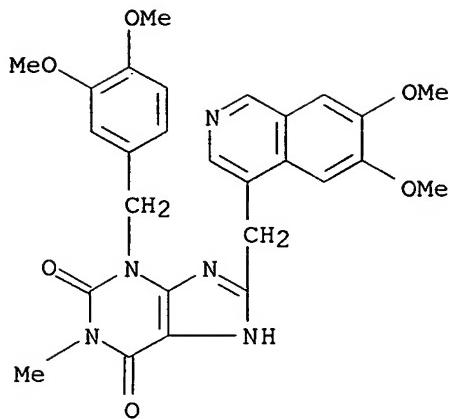
RN 366444-68-0 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3-hexyl-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

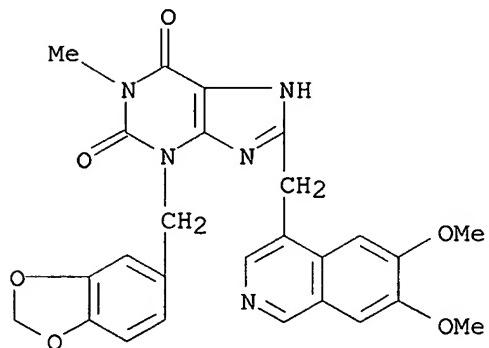


RN 366444-69-1 HCAPLUS

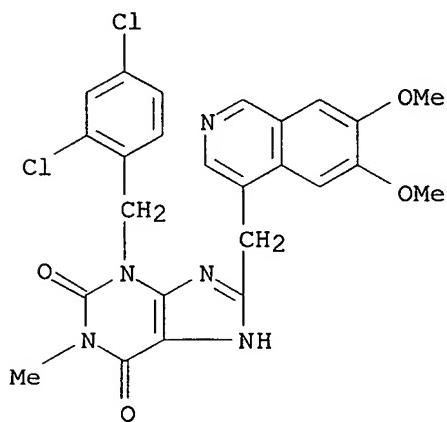
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3-[(3,4-dimethoxyphenyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 366444-70-4 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3-[(1,3-benzodioxol-5-ylmethyl)-8-[(6,7-dimethoxy-4-isooquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

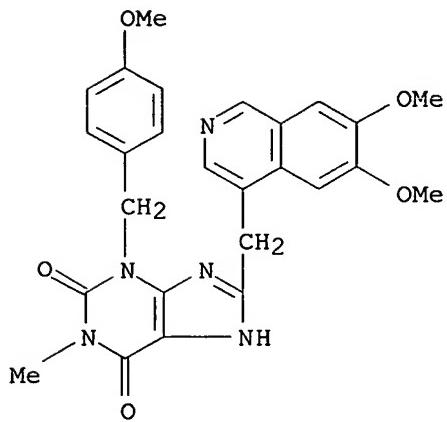


RN 366444-71-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3-[(2,4-dichlorophenyl)methyl]-8-[(6,7-dimethoxy-4-isooquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



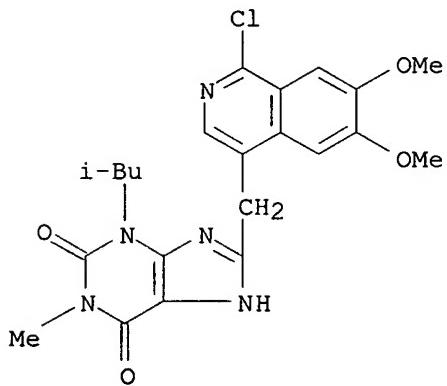
RN 366444-72-6 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isooquinolinyl)methyl]-3,7-dihydro-

3-[ (4-methoxyphenyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



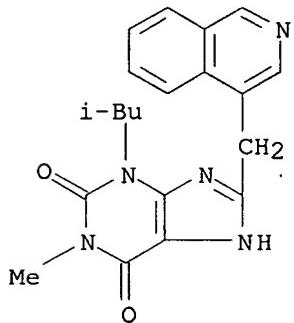
RN 366444-73-7 HCPLUS

CN 1H-Purine-2,6-dione, 8-[ (1-chloro-6,7-dimethoxy-4-isquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366444-74-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-isquinolinylmethyl)-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

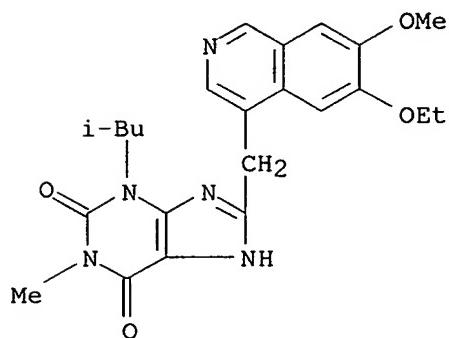


RN 366444-75-9 HCPLUS

CN 1H-Purine-2,6-dione, 8-[ (6-ethoxy-7-methoxy-4-isquinolinyl)methyl]-3,7-

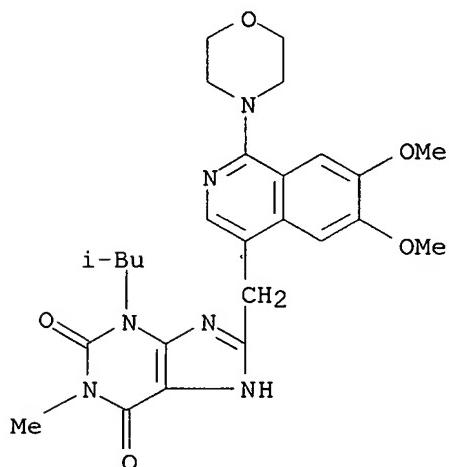
Searched by: Mary Hale 308-4258 CM-1 1E01

dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



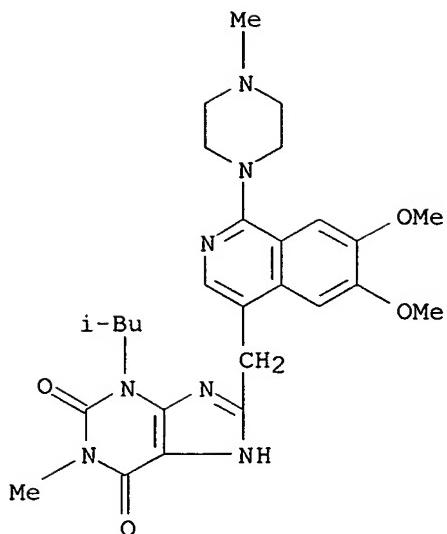
RN 366444-76-0 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-1-(4-morpholinyl)-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



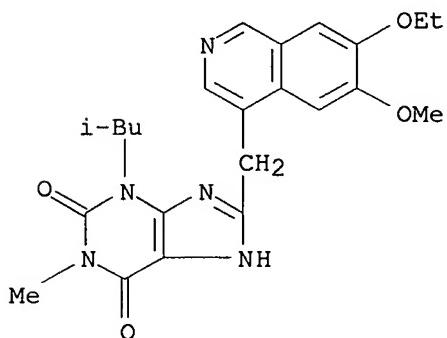
RN 366444-77-1 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-1-(4-methyl-1-piperazinyl)-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



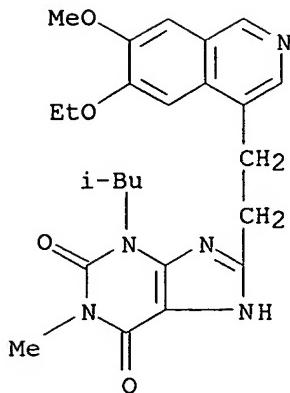
RN 366444-78-2 HCPLUS

CN 1H-Purine-2,6-dione, 8-[ (7-ethoxy-6-methoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



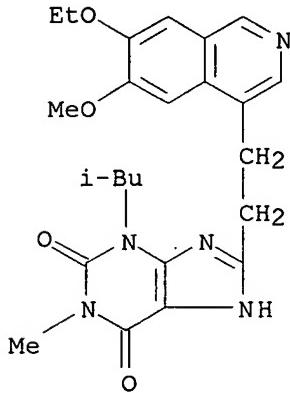
RN 366444-79-3 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(6-ethoxy-7-methoxy-4-isoquinolinyl)ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



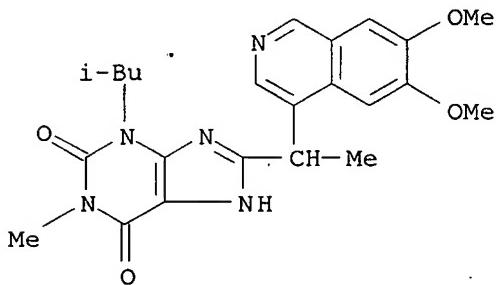
RN 366444-80-6 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(7-ethoxy-6-methoxy-4-isoquinolinyl)ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



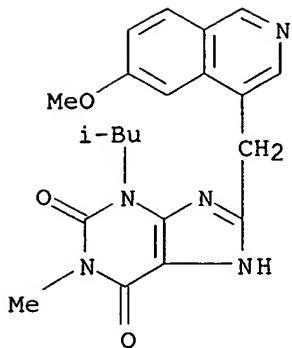
RN 366444-81-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[1-(6,7-dimethoxy-4-isoquinolinyl)ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366444-83-9 HCAPLUS

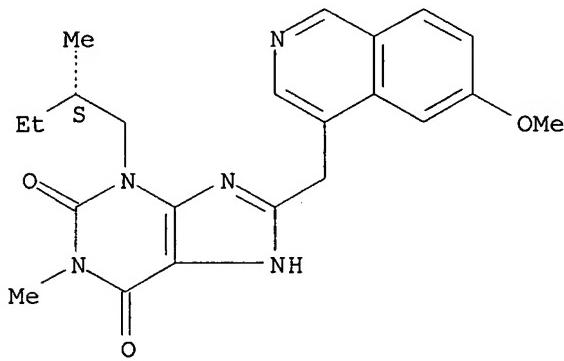
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366444-84-0 HCPLUS

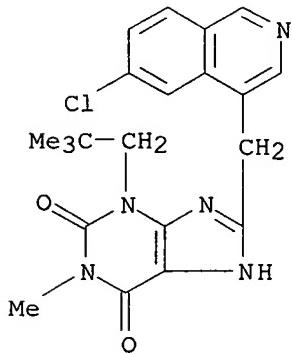
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-3-[(2S)-2-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



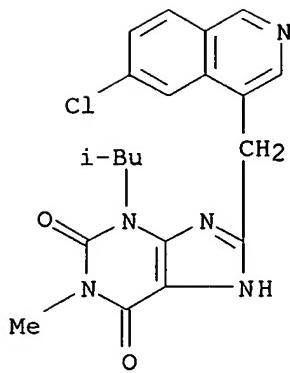
RN 366444-85-1 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(6-chloro-4-isoquinolinyl)methyl]-3-(2,2-dimethylpropyl)-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



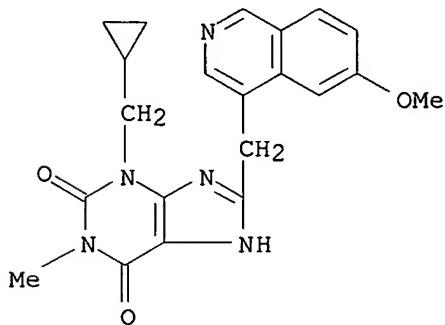
RN 366444-86-2 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(6-chloro-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



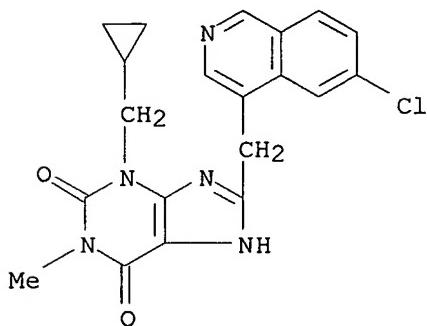
RN 366444-87-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3-(cyclopropylmethyl)-3,7-dihydro-8-[(6-methoxy-4-isquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



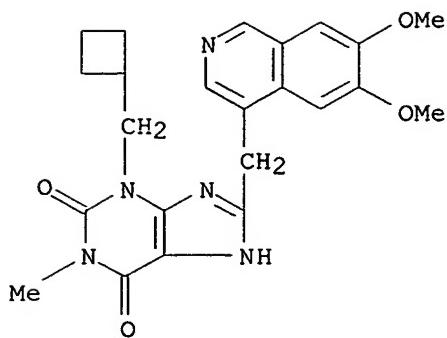
RN 366444-88-4 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(6-chloro-4-isquinolinyl)methyl]-3-(cyclopropylmethyl)-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



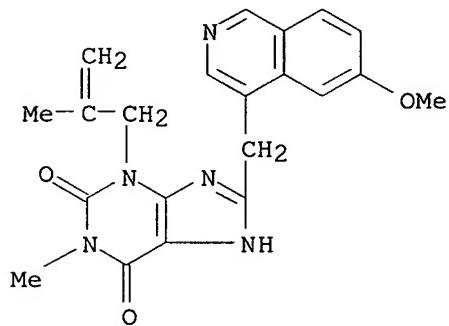
RN 366444-89-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3-(cyclobutylmethyl)-8-[(6,7-dimethoxy-4-isquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



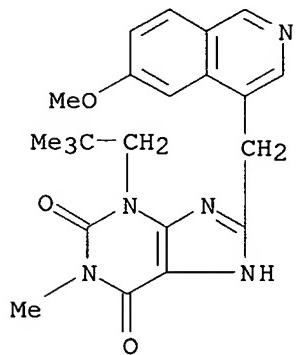
RN 366444-90-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-3-(2-methyl-2-propenyl)- (9CI) (CA INDEX NAME)



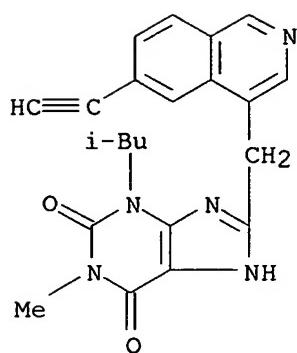
RN 366444-92-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3-(2,2-dimethylpropyl)-3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



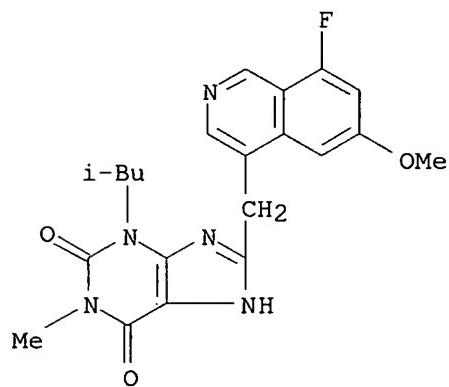
RN 366444-93-1 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(6-ethynyl-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



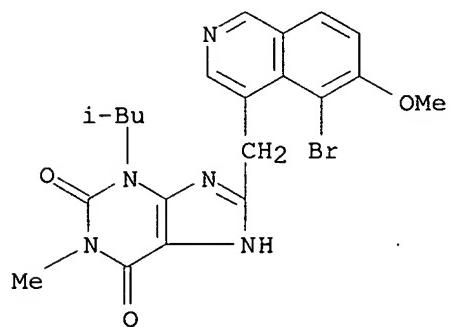
RN 366444-94-2 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(8-fluoro-6-methoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



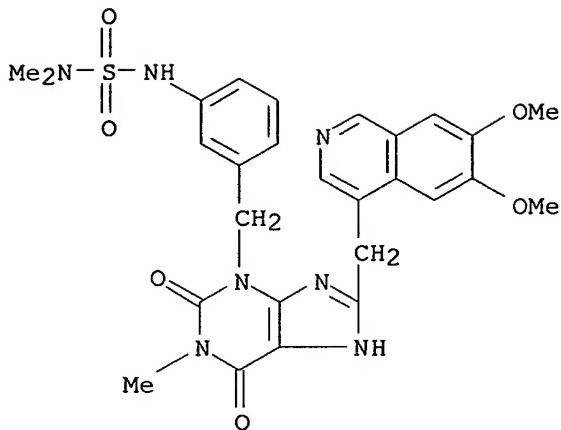
RN 366444-95-3 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(5-bromo-6-methoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



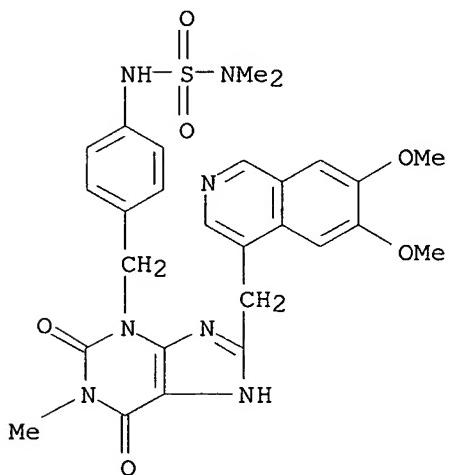
RN 366444-97-5 HCPLUS

CN Sulfamide, N'-[3-[[8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



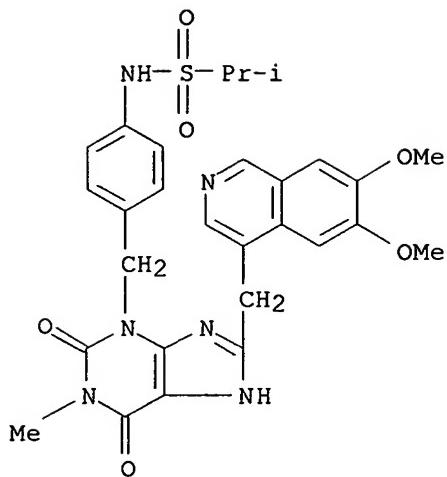
RN 366444-98-6 HCPLUS

CN Sulfamide, N'-[4-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



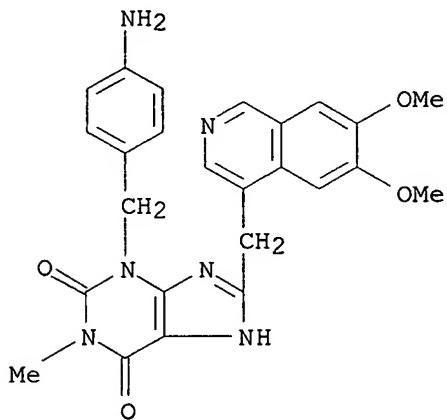
RN 366444-99-7 HCPLUS

CN 2-Propanesulfonamide, N-[4-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-1,2,6,7-tetrahydro-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



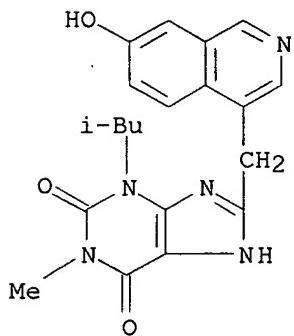
RN 366445-00-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3-[(4-aminophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

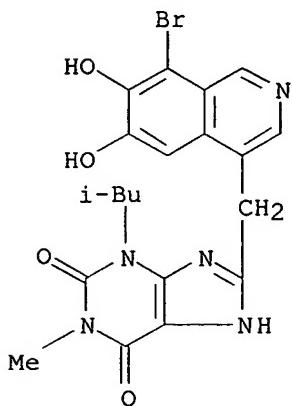


RN 366445-01-4 HCAPLUS

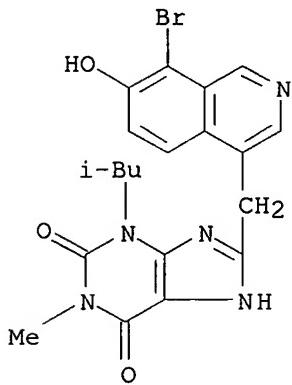
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(7-hydroxy-4-isoquinolinyl)methyl]-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



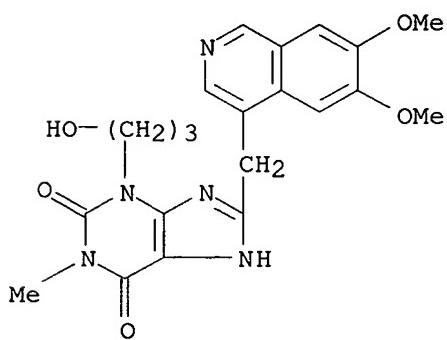
RN 366445-03-6 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[(8-bromo-6,7-dihydroxy-4-isquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



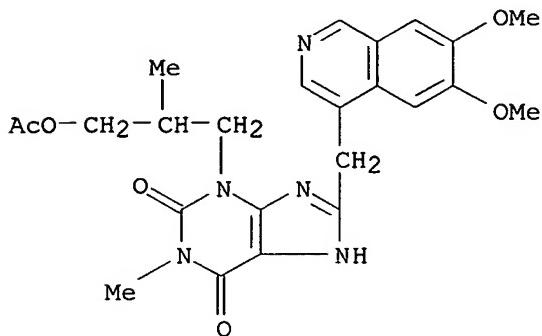
RN 366445-04-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[(8-bromo-7-hydroxy-4-isquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



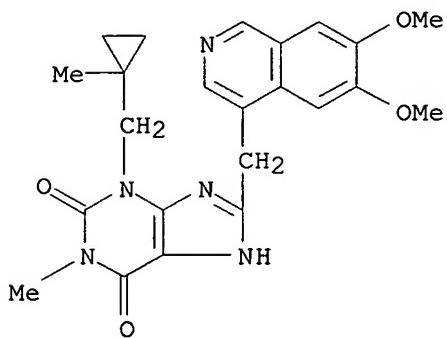
RN 366445-05-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isquinolinyl)methyl]-3,7-dihydro-3-(3-hydroxypropyl)-1-methyl- (9CI) (CA INDEX NAME)



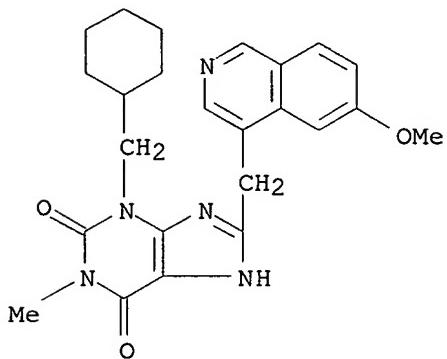
RN 366445-07-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 3-[3-(acetyloxy)-2-methylpropyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 366445-08-1 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-[(1-methylcyclopropyl)methyl]- (9CI) (CA INDEX NAME)



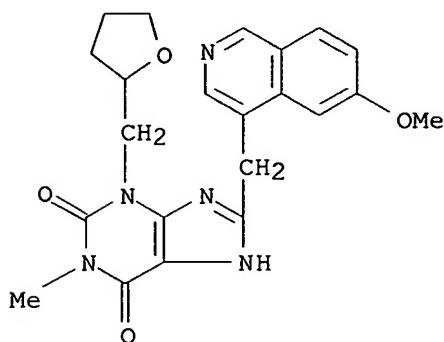
RN 366445-09-2 HCAPLUS  
CN 1H-Purine-2,6-dione, 3-(cyclohexylmethyl)-3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



RN 366445-10-5 HCAPLUS

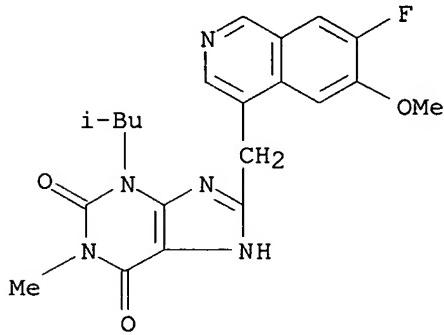
Searched by: Mary Hale 308-4258 CM-1 1E01

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-3-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



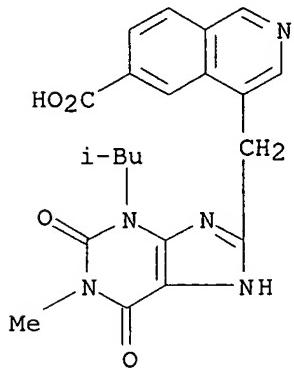
RN 366445-11-6 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(7-fluoro-6-methoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



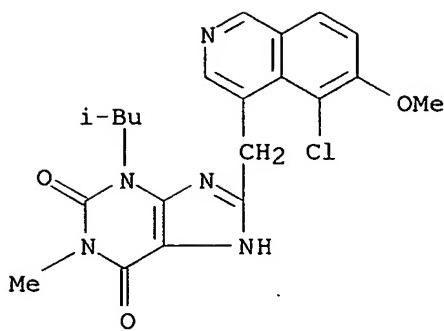
RN 366445-12-7 HCPLUS

CN 6-Isoquinolinecarboxylic acid, 4-[[2,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-2,6-dioxo-1H-purin-8-yl]methyl]- (9CI) (CA INDEX NAME)



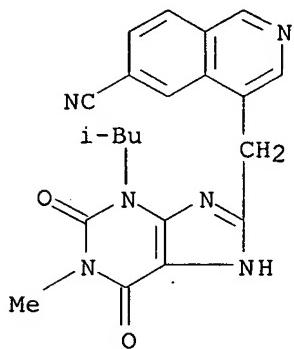
RN 366445-13-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(5-chloro-6-methoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



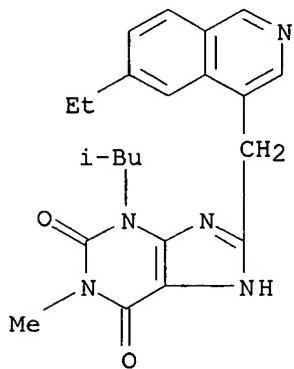
RN 366445-14-9 HCPLUS

CN 6-Isoquinolinecarbonitrile, 4-[(2,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-2,6-dioxo-1H-purin-8-yl)methyl]- (9CI) (CA INDEX NAME)



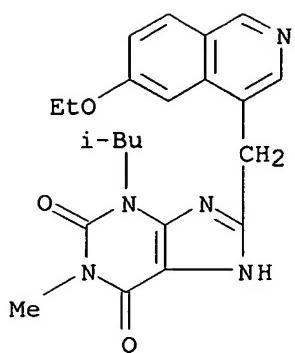
RN 366445-15-0 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(6-ethyl-4-isooquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



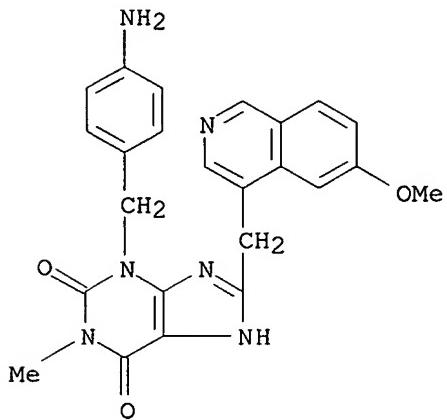
RN 366445-16-1 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(6-ethoxy-4-isooquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



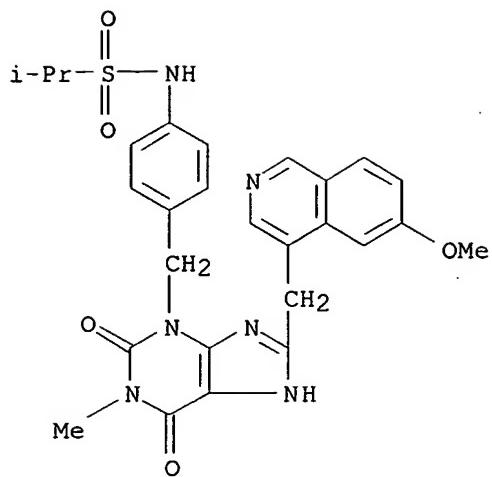
RN 366445-17-2 HCAPLUS

CN 1H-Purine-2,6-dione, 3-[(4-aminophenyl)methyl]-3,7-dihydro-8-[(6-methoxy-4-isooquinolinyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



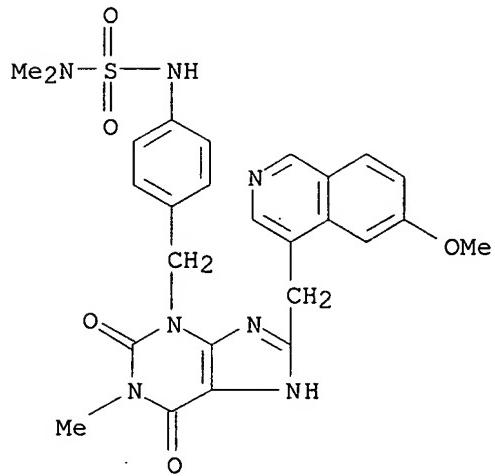
RN 366445-18-3 HCAPLUS

CN 2-Propanesulfonamide, N-[4-[(1,2,6,7-tetrahydro-8-[(6-methoxy-4-isooquinolinyl)methyl]-1-methyl-2,6-dioxo-3H-purin-3-yl)methyl]phenyl]- (9CI) (CA INDEX NAME)



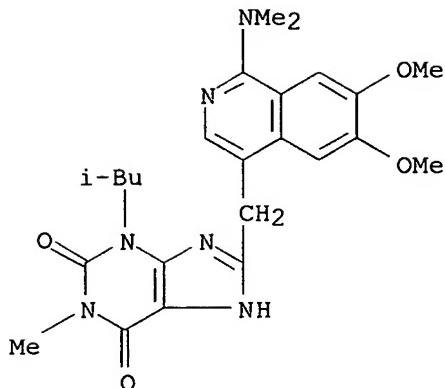
RN 366445-19-4 HCAPLUS

CN Sulfamide, N,N-dimethyl-N'-(4-[[1,2,6,7-tetrahydro-8-[(6-methoxy-4-isoquinolinyl)methyl]-1-methyl-2,6-dioxo-3H-purin-3-yl]methyl]phenyl)-(9CI) (CA INDEX NAME)



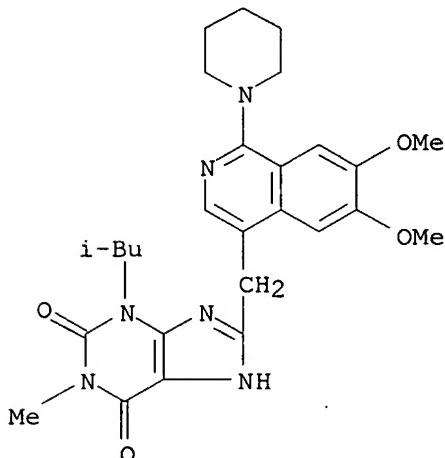
RN 366445-20-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[[1-(dimethylamino)-6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)-(9CI) (CA INDEX NAME)



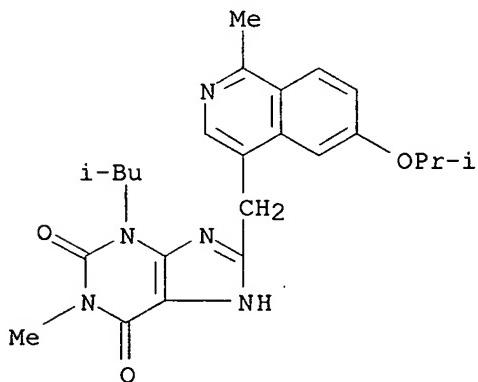
RN 366445-21-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-1-(1-piperidinyl)-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

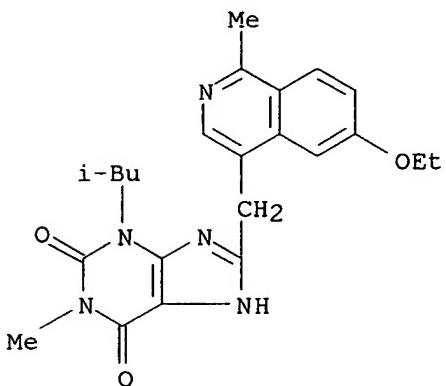


RN 366445-22-9 HCAPLUS

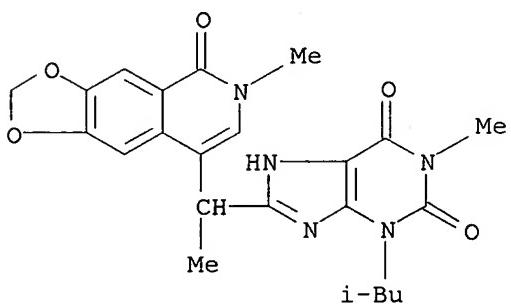
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-8-[[1-methyl-6-(1-methylethoxy)-4-isoquinolinyl]methyl]-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



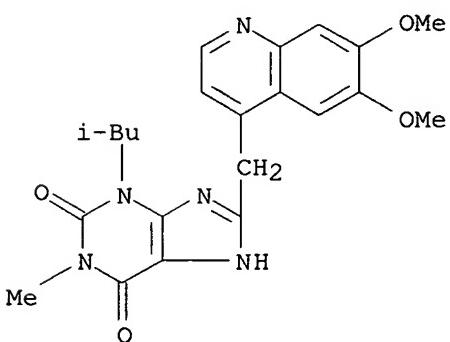
RN 366445-23-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[(6-ethoxy-1-methyl-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366445-24-1 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[1-(5,6-dihydro-6-methyl-5-oxo-1,3-dioxolo[4,5-g]isoquinolin-8-yl)ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



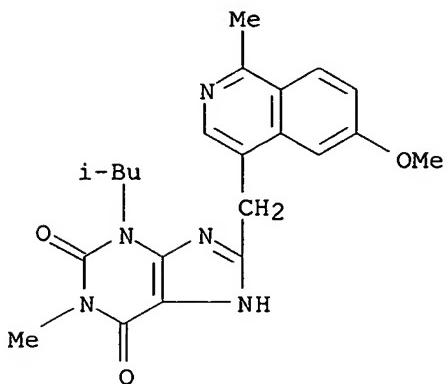
RN 366445-25-2 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[(6,7-dimethoxy-4-quinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366445-26-3 HCAPLUS

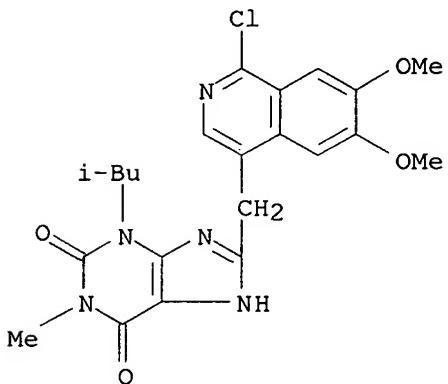
Searched by: Mary Hale 308-4258 CM-1 1E01

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(6-methoxy-1-methyl-4-isoquinolinyl)methyl]-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 366446-17-5 HCPLUS

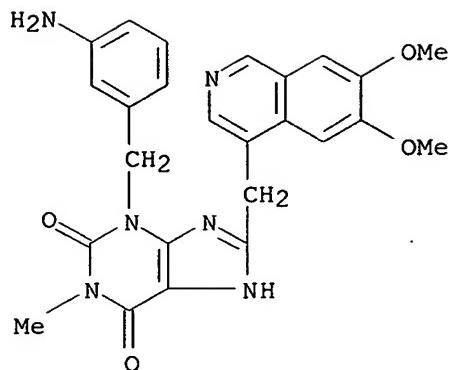
CN 1H-Purine-2,6-dione, 8-[(1-chloro-6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 366446-18-6 HCPLUS

CN 1H-Purine-2,6-dione, 3-[(3-aminophenyl)methyl]-8-[(6,7-dimethoxy-4-isoquinolinyl)methyl]-3,7-dihydro-1-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

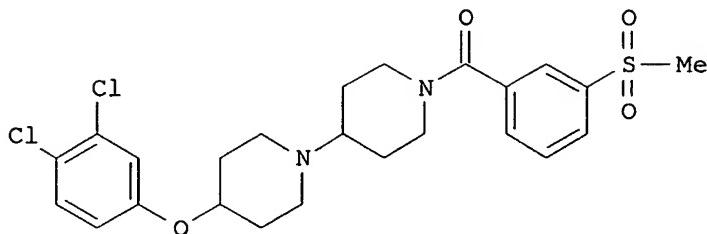
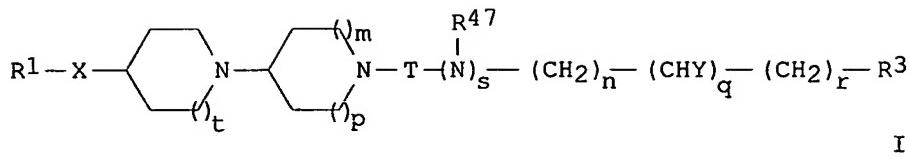


● 2 HCl

L5 ANSWER 12 OF 163 HCPLUS COPYRIGHT 2002 ACS

2001:762989 Document No. 135:318419 Synthesis of substituted bipiperidines and their use as H1 antagonists. Lawrence, Louise; Rigby, Aaron; Sangane, Hitesh; Springthorpe, Brian (Astrazeneca AB, Swed.). PCT Int. Appl. WO 2001077101 A1 20011018, 160 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-SE751 20010405. PRIORITY: GB 2000-8626 20000408; GB 2000-19111 20000803; SE 2000-3664 20001011.

GI



AB Title compds. I [q, s, t = 0 - 1; n, r = 0 - 5; m, p = 0 - 2; X = CH, C(O), O, S, S(O), S(O), N-; provided that when m and p are both 1 then X is not CH; Y = NHR<sub>2</sub>, OH; T = C(O), C(S), S(O), CH<sub>2</sub>; R<sub>1</sub> = H, alkyl, aryl, heterocyclyl; R<sub>2</sub>, R<sub>47</sub> = H, alkyl, aryl-alkyl, CO-alkyl; R<sub>3</sub> = alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heterocyclyl, thioaryl, thioheterocyclyl] were prepd. Examples include: data for over 600 compds., 4 solid oral dosage and 1 parenteral (general) formulations, a bioassay for Ca<sup>2+</sup> flux, human eosinophil chemotaxis and H<sub>1</sub> antagonism. E.g., 4-(3,4-dichlorophenoxy)piperidine was alkylated with 1-(tert-butoxycarbonyl)-4-piperidone (1,2-dichloroethane, NaBH(OAc)<sub>3</sub>, HOAc, 18 h, room temp.) to give an intermediate [1,4']bipiperidine. This intermediate was deprotected (DCM, TFA, 4 h, room temp.) and the resulting bipiperidine condensed with 3-methanesulfonylbenzoic acid (THF, PYBROP, (i-Pr)<sub>2</sub>NEt, 18 h, room temp.) to give example compd. II isolated as the acetate salt. I are used in the treatment of a chemokine (such as CCR3) or H<sub>1</sub> mediated disease state.

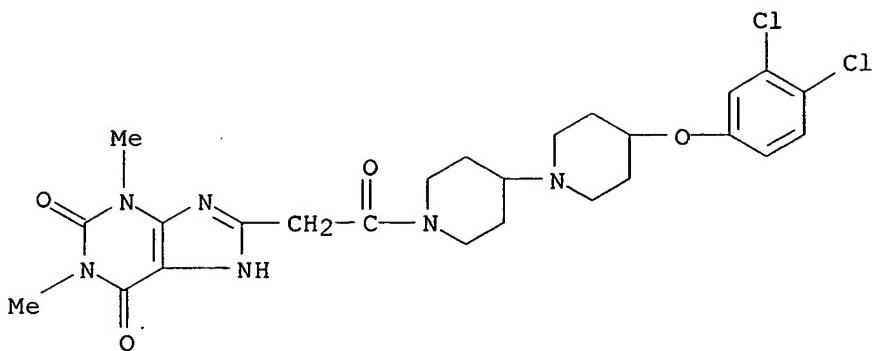
IT **367497-54-9P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(drug; synthesis of substituted bipiperidines and use as H1 antagonists)

BN 367487 54 8 HCAHHS

RN 367497-34-9 HCAPLUS  
CN 1,4'-Bipiperidine, 4-(3,4-dichlorophenoxy)-1'-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)acetyl- (9CI) (CA INDEX NAME)

BN 367487 54 8 HCAHHS

RN 367497-34-9 HCAPLUS  
CN 1,4'-Bipiperidine, 4-(3,4-dichlorophenoxy)-1'-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)acetyl- (9CI) (CA INDEX NAME)



L5 ANSWER 13 OF 163 HCPLUS COPYRIGHT 2002 ACS

2001:678215 Document No. 136:47 Renal effects of adenosine A<sub>1</sub>-receptor antagonists in congestive heart failure. Gottlieb, Stephen S. (Division of Cardiology, University of Maryland School of Medicine, Baltimore, MD, USA). Drugs, 61(10), 1387-1393 (English) 2001. CODEN: DRUGAY. ISSN: 0012-6667. Publisher: Adis International Ltd..

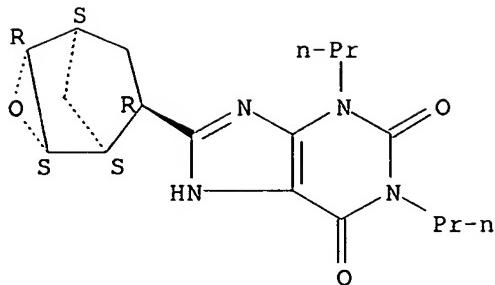
AB A review with refs. Renal function is a very important prognostic indicator in patients with congestive heart failure. While some of the prognostic importance of poor renal function is related to the worse physiol. assocd. with it, there are suggestions that the dysfunction itself is detrimental. Recently, it has been shown that adenosine may mediate much kidney activity. In addn. to vasoconstrictive and vasodilatory effects, adenosine is intrinsic to the tubuloglomerular feedback which occurs when an acute increase in sodium levels in the proximal tubule feeds back to decrease glomerular filtration. Adenosine works via both adenosine A<sub>1</sub> and A<sub>2</sub> receptors. A<sub>1</sub>-receptor antagonists decrease afferent arteriolar pressure, and increase urine flow and sodium excretion. Studies suggest that A<sub>1</sub>-receptor antagonists cause a diuretic effect not by a change in the renal hemodynamics, but by the inhibition of water and sodium reabsorption in tubular sites secondary to direct tubuloglomerular feedback. Less consistent has been the occasional finding of increased glomerular filtration rate despite the lack of improved renal plasma flow. Clin. important questions are: what role adenosine plays in causing the poor renal function assocd. with heart failure and what A<sub>1</sub>-receptor antagonists do in such situations If an A<sub>1</sub>-receptor antagonist could cause diuresis while maintaining or improving glomerular filtration, it would be a useful adjunct in the treatment of severe heart failure. We evaluated the effects of the A<sub>1</sub>-receptor antagonist CVT-124 (BG-9719) in heart failure patients. CVT-124 increased sodium excretion without decreasing glomerular filtration rate. These data suggest that adenosine might be an important determinant of renal function in patients with heart failure.

IT 166374-48-7, CVT-124  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (renal effects of adenosine A<sub>1</sub>-receptor antagonists in humans with congestive heart failure)

RN 166374-48-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 14 OF 163 HCPLUS COPYRIGHT 2002 ACS

2001:617805 Document No. 135:175381 Method for identifying and using A2b adenosine receptor antagonists to mediate mammalian cell proliferation. Belardinelli, Luiz; Grant, Maria B. (CV Therapeutics, Inc., USA; University of Florida Research Foundation, Inc.). PCT Int. Appl. WO 2001060350 A2 20010823, 17 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US4917 20010216. PRIORITY: US 2000-PV183141 20000217.

AB This invention concerns methods for identifying A2B adenosine receptor agonists and antagonists as well as methods for using A2B adenosine receptor antagonists to treat cell proliferation orders mediated by the A2B adenosine receptor.

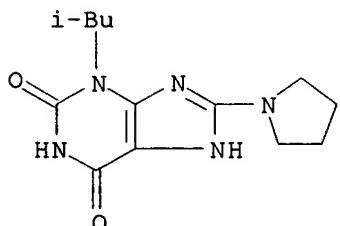
IT 329024-77-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method for identifying and using A2b adenosine receptor antagonists to mediate mammalian cell proliferation)

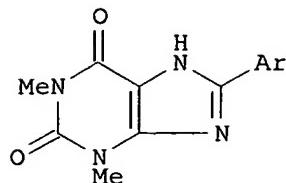
RN 329024-77-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-(2-methylpropyl)-8-(1-pyrrolidinyl)-(9CI) (CA INDEX NAME)



L5 ANSWER 15 OF 163 HCPLUS COPYRIGHT 2002 ACS

2001:577272 Document No. 136:340647 Synthesis of 3,7-dihydro-1,3-dimethyl-1H-purine-2,6-dione derivatives as potentially biologically active substances. Bratulescu, G. (Universite de Craiova, Faculte de Chimie, Departement de Chimie Organique, Craiova, 110, Rom.). Journal de la Societe Algerienne de Chimie, 11(1), 115-119 (French) 2001. CODEN:



I

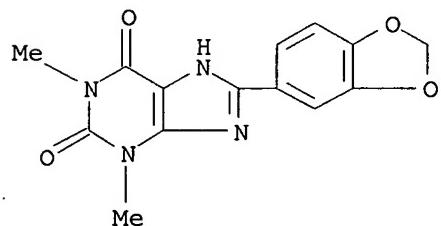
AB Seven new theophilline derivs. [I; Ar = 2-furanyl, benzo[b]furan-2-yl, (un)substituted phenyl] were synthesized by reaction of 5,6-diamino-1,3-dimethyluracil with arom. carboxylic acid chlorides. The structures of the synthesized compds. were confirmed by elemental anal. and 1H NMR spectral anal.

IT 20886-69-5P 33797-74-9P 166115-58-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

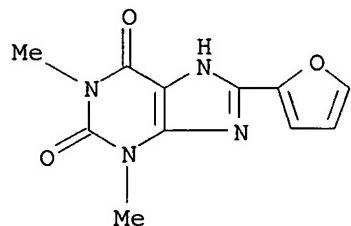
RN 20886-69-5 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(1,3-benzodioxol-5-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



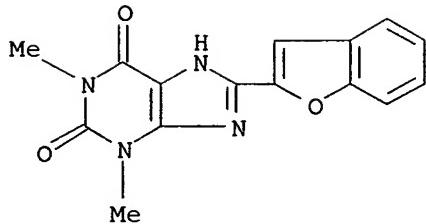
RN 33797-74-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 166115-58-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-benzofuranyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

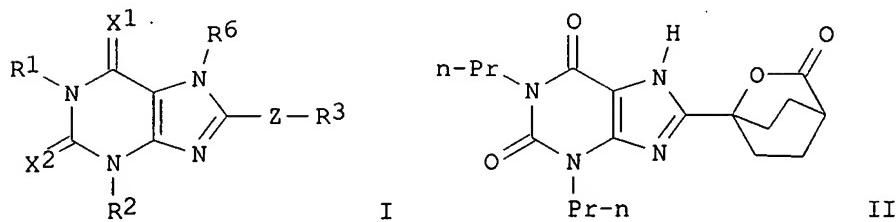


L5 ANSWER 16 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2001:360002 Document No. 134:366889 Preparation of polycycloalkylpurines as adenosine receptor antagonists. Kiesman, William F.; Dowling, James E.; Ensinger, Carol L.; Kumaravel, Gnanasambandam; Petter, Russell C.; Chang, He Xi; Lin, Ko Chung (Biogen, Inc., USA). PCT Int. Appl. WO 2001034610 A1 20010517, 124 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.

APPLICATION: WO 2000-US31058 20001113. PRIORITY: US 1999-PV165191 19991112.

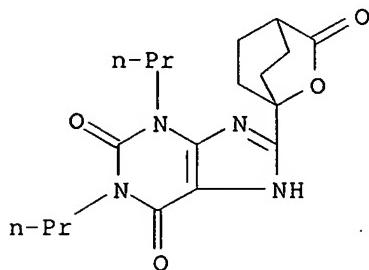
GI



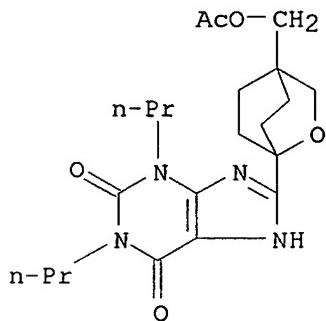
AB The title compds. [I; R1, R2 = H, alkyl, alkenyl, etc.; R3 = (un)substituted bicyclic, tricyclic, pentacyclic; X1, X2 = = O, S; Z = a single bond, O, CH<sub>2</sub>OCH<sub>2</sub>, etc.; R6 = H, allyl, acyl, etc.] which are unexpectedly highly potent and selective inhibitors of the adenosine A<sub>1</sub> receptor, and therefore can be useful in the prevention and/or treatment of numerous diseases, including cardiac and circulatory disorders, degenerative disorders of the central nervous system, respiratory disorders, and many diseases for which diuretic treatment is suitable, were prep'd. E.g., a multi-step synthesis of the purine II was given. All of the compds. I tested exhibited rat A<sub>1</sub> Ki values between 0.6 and 433.8 nM, human A<sub>1</sub> Ki values between 1.6 and 1000 nM, and human A<sub>2a</sub> Ki values between 132 and 49930 nM.

IT 340020-84-0P, 8-(3-Oxo-2-oxabicyclo[2.2.2]oct-1-yl)-1,3-dipropyl-3,7-dihydropurine-2,6-dione 340020-86-2P 340020-87-3P  
 340020-89-5P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

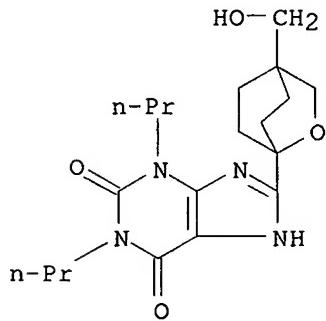
(prep. of polycycloalkylpurines as adenosine receptor antagonists)  
RN 340020-84-0 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxo-2-oxabicyclo[2.2.2]oct-1-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



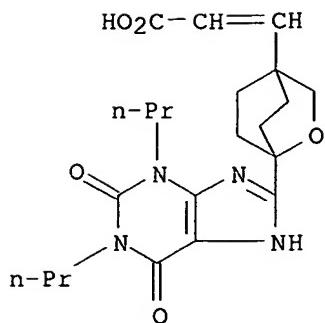
RN 340020-86-2 HCPLUS  
CN 1H-Purine-2,6-dione, 8-[4-[(acetyloxy)methyl]-2-oxabicyclo[2.2.2]oct-1-yl]-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 340020-87-3 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[4-(hydroxymethyl)-2-oxabicyclo[2.2.2]oct-1-yl]-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 340020-89-5 HCPLUS  
CN 2-Propenoic acid, 3-[1-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-2-oxabicyclo[2.2.2]oct-4-yl]- (9CI) (CA INDEX NAME)

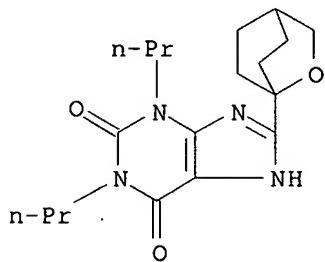


IT 340020-85-1P 340020-88-4P 340020-90-8P  
 340020-92-0P 340020-94-2P 340021-02-5P  
 340021-96-7P 340022-14-2P 340022-15-3P  
 340022-16-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of polycycloalkylpurines as adenosine receptor antagonists)

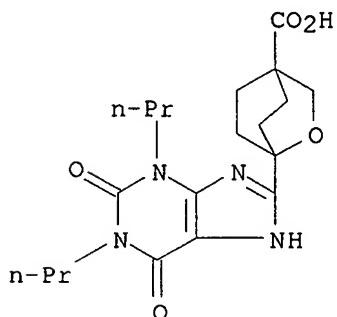
RN 340020-85-1 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(2-oxabicyclo[2.2.2]oct-1-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



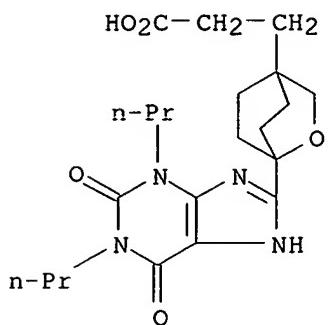
RN 340020-88-4 HCAPLUS

CN 2-Oxabicyclo[2.2.2]octane-4-carboxylic acid, 1-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)

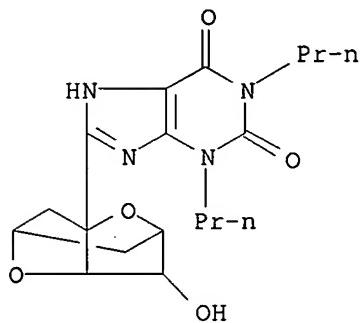


RN 340020-90-8 HCAPLUS

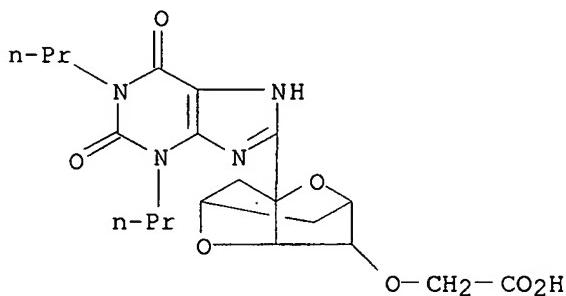
CN 2-Oxabicyclo[2.2.2]octane-4-propanoic acid, 1-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



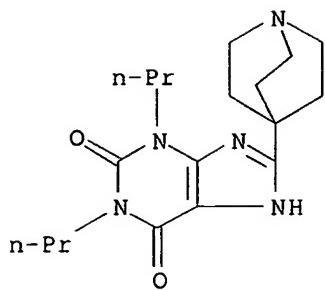
RN 340020-92-0 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(tetrahydro-6-hydroxy-2,5-methanofuro[3,2-b]furan-3a(5H)-yl)- (9CI) (CA INDEX NAME)



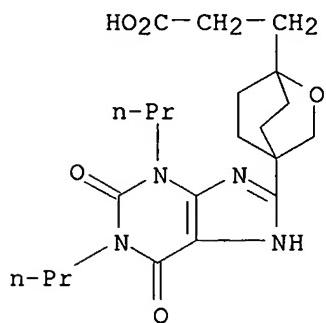
RN 340020-94-2 HCAPLUS  
 CN Acetic acid, [hexahydro-6a-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-2,5-methanofuro[3,2-b]furan-3-yl]oxy]- (9CI) (CA INDEX NAME)



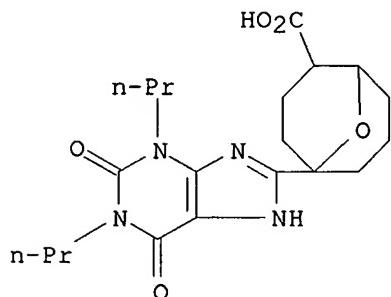
RN 340021-02-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-(1-azabicyclo[2.2.2]oct-4-yl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



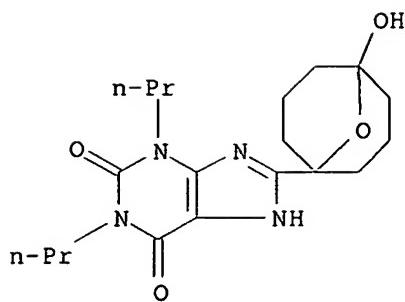
RN 340021-96-7 HCAPLUS  
 CN 2-Oxabicyclo[2.2.2]octane-1-propanoic acid, 4-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



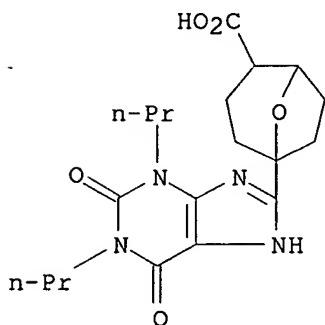
RN 340022-14-2 HCAPLUS  
 CN 9-Oxabicyclo[3.3.1]nonane-2-carboxylic acid, 5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



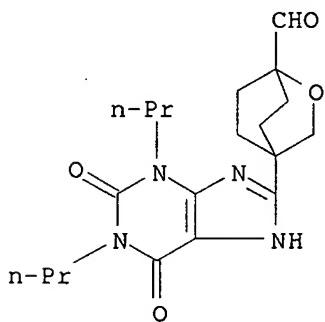
RN 340022-15-3 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(5-hydroxy-9-oxabicyclo[3.3.1]non-1-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



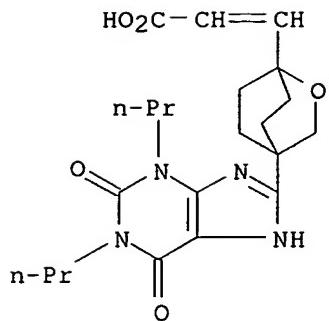
RN 340022-16-4 HCPLUS  
 CN 8-Oxabicyclo[3.2.1]octane-2-carboxylic acid, 5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



IT 340023-22-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
     (prepn. of polycycloalkylpurines as adenosine receptor antagonists)  
 RN 340023-22-5 HCPLUS  
 CN 2-Oxabicyclo[2.2.2]octane-1-carboxaldehyde, 4-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)

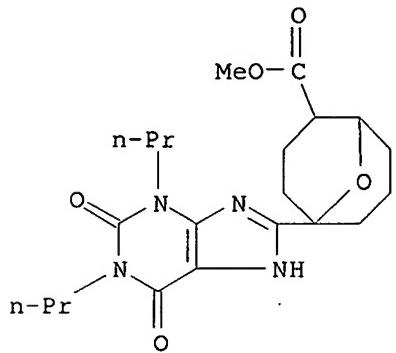


IT 340023-05-4P 340023-07-6P 340025-91-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
     (Reactant or reagent)  
     (prepn. of polycycloalkylpurines as adenosine receptor antagonists)  
 RN 340023-05-4 HCPLUS  
 CN 2-Propenoic acid, 3-[4-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-2-oxabicyclo[2.2.2]oct-1-yl]- (9CI) (CA INDEX NAME)



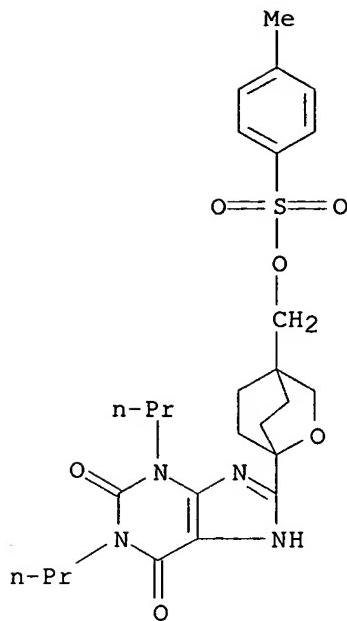
RN 340023-07-6 HCAPLUS

CN 9-Oxabicyclo[3.3.1]nonane-2-carboxylic acid, 5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-, methyl ester (9CI) (CA INDEX NAME)



RN 340025-91-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[4-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-2-oxabicyclo[2.2.2]oct-1-yl]-1,3-dipropyl- (9CI) (CA INDEX NAME)

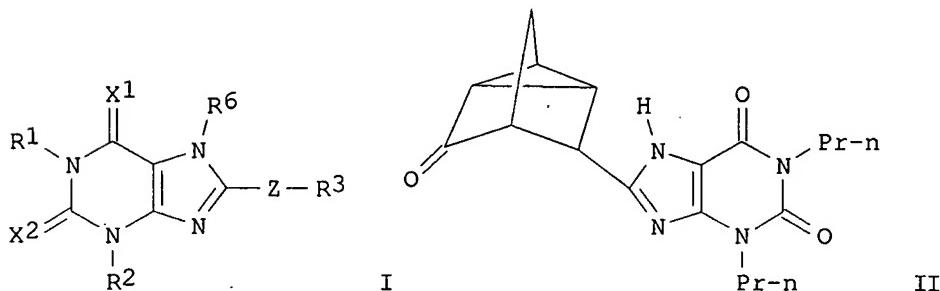


L5 ANSWER 17 OF 163 HCPLUS COPYRIGHT 2002 ACS

2001:359996 Document No. 134:366887 Preparation of 8-substituted xanthines as adenosine receptor antagonists. Dowling, James E.; Ensinger, Carol; Kumaravel, Gnanasambandam; Petter, Russell C. (Biogen, Inc., USA). PCT Int. Appl. WO 2001034604 A2 20010517, 61 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US31100 20001113.

PRIORITY: US 1999-PV165283 19991112.

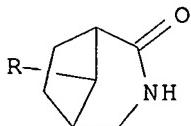
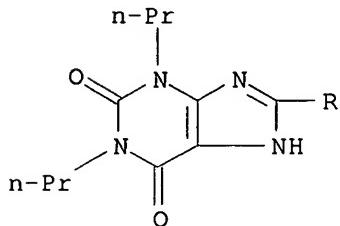
GI



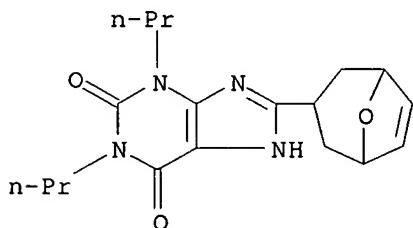
AB The title compds. [I; R1, R2 = H, alkyl, alkenyl, etc.; R3 = (un)substituted bicyclic or tricyclic group; X1, X2 = O, S; Z = a single bond, O, (CH2)1-3, etc.; R6 = H, alkyl, acyl, etc.] which are unexpectedly highly potent and selective inhibitors of the adenosine A1 receptor, and

therefore are useful in the prevention and/or treatment of numerous diseases, including cardiac and circulatory disorders, degenerative disorders of the central nervous system, respiratory disorders, and many diseases for which diuretic treatment is suitable, were prepd. E.g., a 2-step synthesis of II was given. All of the compds. I tested exhibited rat A1 Ki values between 0.47 and 1225 nM, human A1 Ki values between 12 and 1000 nM, and human A2a Ki values between 18 and 100,000 nM.

IT 340163-16-8P 340163-98-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
     (prepn. of 8-substituted xanthines as adenosine receptor antagonists)  
 RN 340163-16-8 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(2-oxo-3-azabicyclo[3.2.1]oct-8-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)

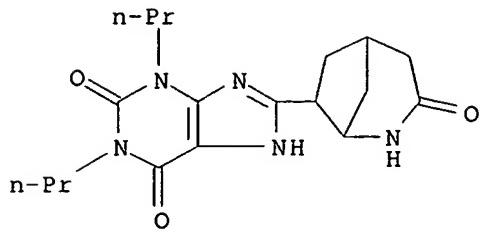


RN 340163-98-6 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(8-oxabicyclo[3.2.1]oct-6-en-3-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)

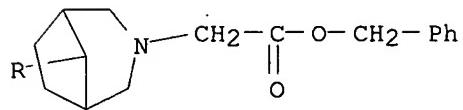
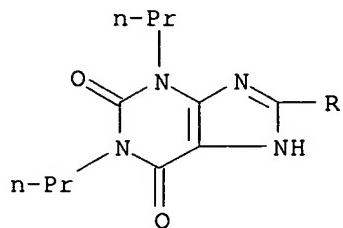


IT 340163-15-7P 340163-17-9P 340163-18-0P  
 340163-49-7P 340163-51-1P 340163-53-3P  
 340163-96-4P 340163-97-5P 340163-99-7P  
 340164-00-3P 340164-01-4P 340266-61-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
     (prepn. of 8-substituted xanthines as adenosine receptor antagonists)  
 RN 340163-15-7 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxo-2-azabicyclo[3.2.1]oct-7-yl)-1,3-

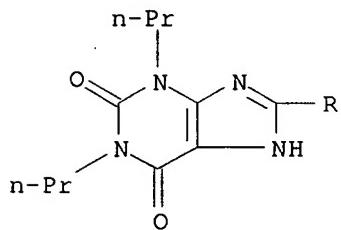
dipropyl- (9CI) (CA INDEX NAME)



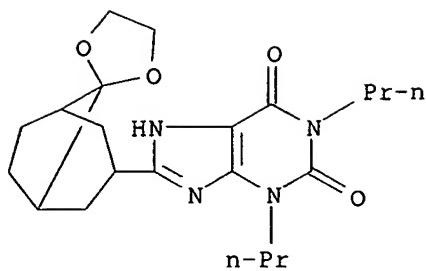
RN 340163-17-9 HCPLUS  
CN 3-Azabicyclo[3.2.1]octane-3-acetic acid, 8-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 340163-18-0 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxo-2-azabicyclo[3.2.1]oct-8-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



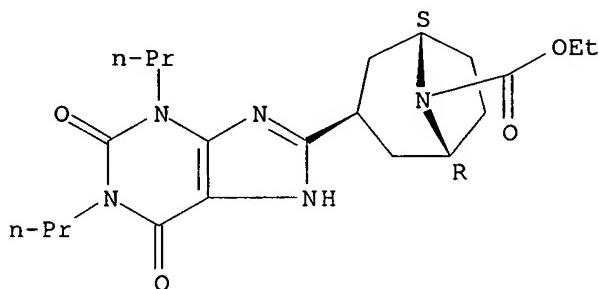
RN 340163-49-7 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-spiro[bicyclo[3.2.1]octane-8,2'-[1,3]dioxolan]-3-yl- (9CI) (CA INDEX NAME)



RN 340163-51-1 HCPLUS

CN 8-Azabicyclo[3.2.1]octane-8-carboxylic acid, 3-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-, ethyl ester, (3-exo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 340163-53-3 HCPLUS

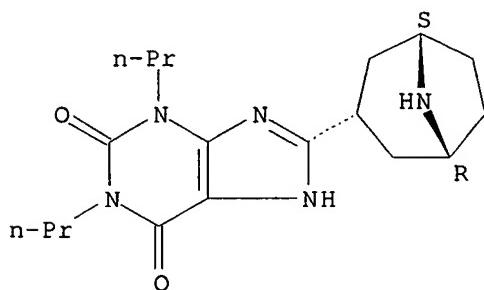
CN 1H-Purine-2,6-dione, 8-(3-endo)-8-azabicyclo[3.2.1]oct-3-yl-3,7-dihydro-1,3-dipropyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 340163-52-2

CMF C18 H27 N5 O2

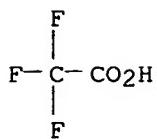
Relative stereochemistry.



CM 2

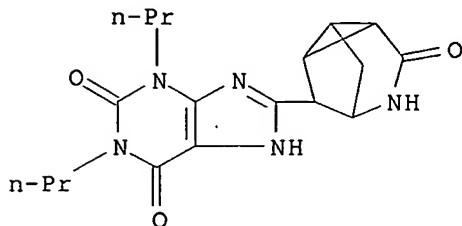
CRN 76-05-1

CMF C2 H F3 O2



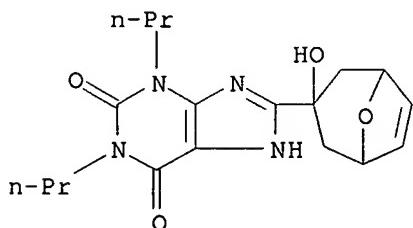
RN 340163-96-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxo-4-azatricyclo[3.2.1.0<sub>2,7</sub>]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



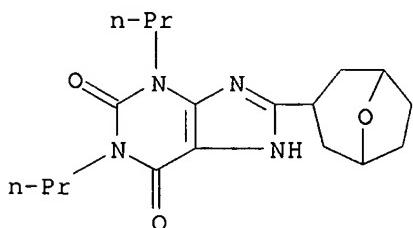
RN 340163-97-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-hydroxy-8-oxabicyclo[3.2.1]oct-6-en-3-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



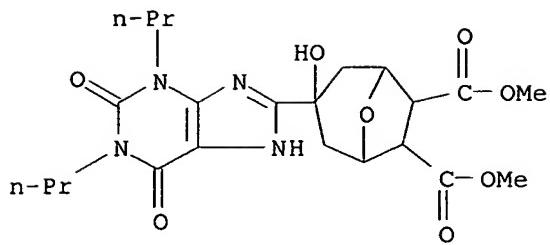
RN 340163-99-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(8-oxabicyclo[3.2.1]oct-3-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



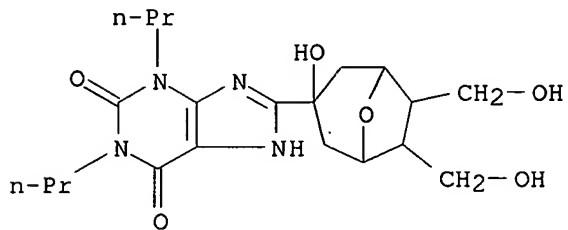
RN 340164-00-3 HCAPLUS

CN 8-Oxabicyclo[3.2.1]octane-6,7-dicarboxylic acid, 3-hydroxy-3-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-, dimethyl ester (9CI) (CA INDEX NAME)



RN 340164-01-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[3-hydroxy-6,7-bis(hydroxymethyl)-8-oxabicyclo[3.2.1]oct-3-yl]-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 340266-61-7 HCAPLUS

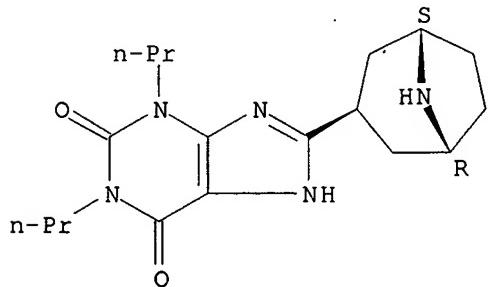
CN 1H-Purine-2,6-dione, 8-(3-exo)-8-azabicyclo[3.2.1]oct-3-yl-3,7-dihydro-1,3-dipropyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 340266-60-6

CMF C18 H27 N5 O2

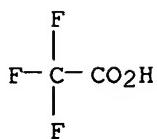
Relative stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

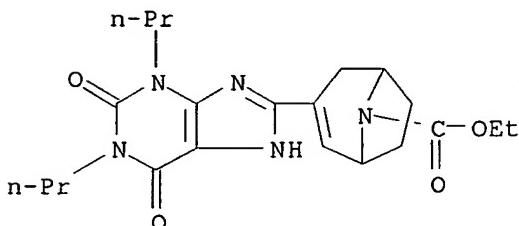


IT 340164-33-2 340255-31-4

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prep. of 8-substituted xanthines as adenosine receptor antagonists)

RN 340164-33-2 HCPLUS

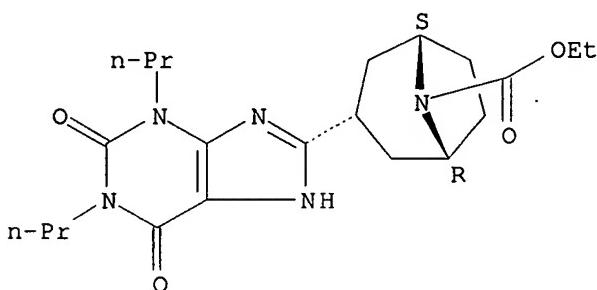
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 3-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 340255-31-4 HCPLUS

CN 8-Azabicyclo[3.2.1]octane-8-carboxylic acid, 3-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-, ethyl ester, (3-endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 18 OF 163 HCPLUS COPYRIGHT 2002 ACS

2001:322259 Document No. 135:55469 Structure-activity relationships in a series of 8-substituted xanthines as A1-adenosine receptor antagonists. Strappaghetti, Giovannella; Corsano, Stefano; Barbaro, Roberta; Giannaccini, Gino; Betti, Laura (Dipartimento di Chimica e Tecnologia del Farmaco, Universita di Perugia, Perugia, 06123, Italy). Bioorganic & Medicinal Chemistry, 9(3), 575-583 (English) 2001. CODEN: BMECEP. ISSN: 0968-0896. Publisher: Elsevier Science Ltd..

AB A series of 8-substituted xanthines were synthesized and their affinity in vitro towards A1, A2A-adenosine receptors was evaluated by radioligand receptor binding assays. All compds. showed a greater affinity and selectivity towards the A1-adenosine receptor than theophylline. The compds. in which the Pr group is in 1-position of the xanthine nucleus and the pyridazinone system in 8-position is linked through a chain of two or

four carbon atoms, showed the highest affinity and selectivity.

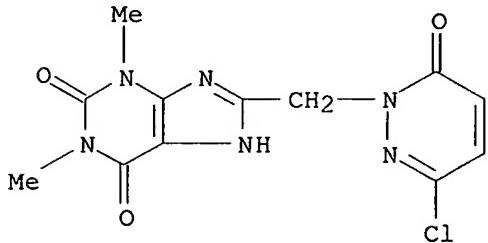
IT 346406-92-6P 346406-93-7P 346406-96-0P  
 346406-97-1P 346407-00-9P 346407-02-1P  
 346407-03-2P 346407-06-5P 346407-07-6P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(structure-activity relationships of 8-substituted xanthines as A<sub>1</sub>-adenosine receptor antagonists)

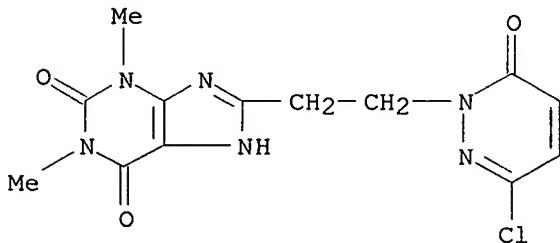
RN 346406-92-6 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(3-chloro-6-oxo-1(6H)-pyridazinyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



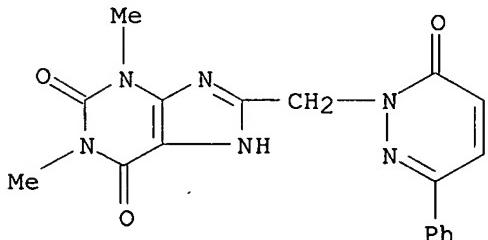
RN 346406-93-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(3-chloro-6-oxo-1(6H)-pyridazinyl)ethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



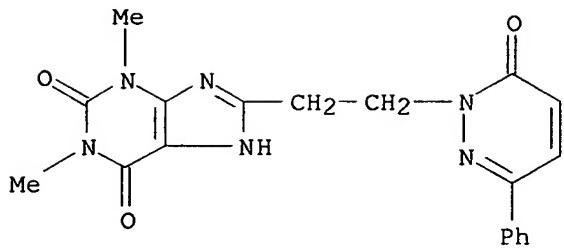
RN 346406-96-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(6-oxo-3-phenyl-1(6H)-pyridazinyl)methyl]- (9CI) (CA INDEX NAME)

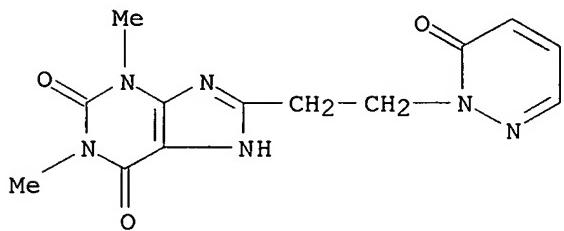


RN 346406-97-1 HCAPLUS

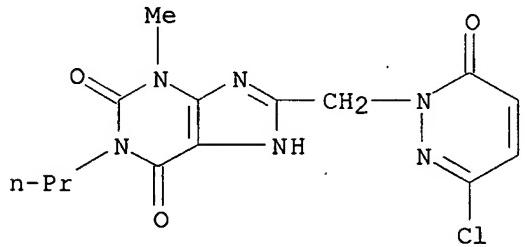
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[2-(6-oxo-3-phenyl-1(6H)-pyridazinyl)ethyl]- (9CI) (CA INDEX NAME)



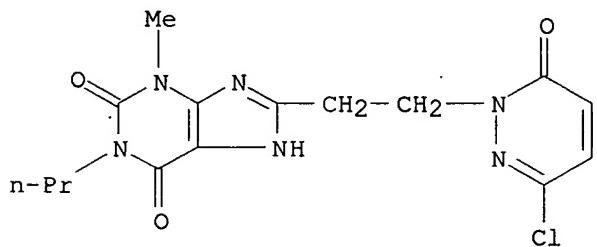
RN 346407-00-9 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[2-(6-oxo-1(6H)-pyridazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 346407-02-1 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[ (3-chloro-6-oxo-1(6H)-pyridazinyl)methyl]-3,7-dihydro-3-methyl-1-propyl- (9CI) (CA INDEX NAME)

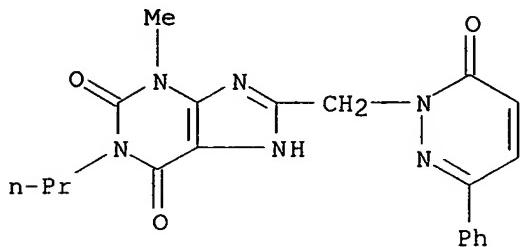


RN 346407-03-2 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-(3-chloro-6-oxo-1(6H)-pyridazinyl)ethyl]-3,7-dihydro-3-methyl-1-propyl- (9CI) (CA INDEX NAME)



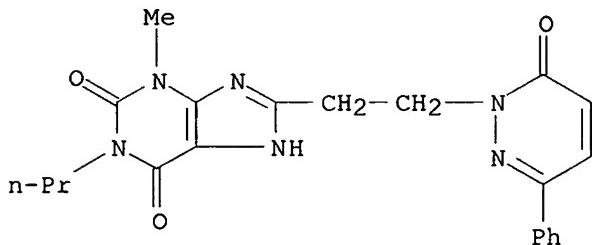
RN 346407-06-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-8-[(6-oxo-3-phenyl-1(6H)-pyridazinyl)methyl]-1-propyl- (9CI) (CA INDEX NAME)



RN 346407-07-6 HCPLUS

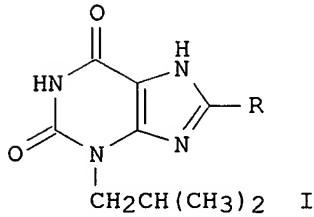
CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-8-[2-(6-oxo-3-phenyl-1(6H)-pyridazinyl)ethyl]-1-propyl- (9CI) (CA INDEX NAME)



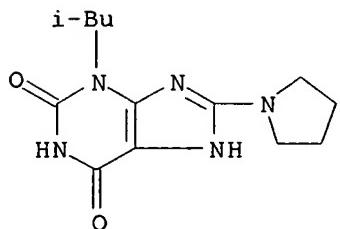
L5 ANSWER 19 OF 163 HCPLUS COPYRIGHT 2002 ACS

2001:167993 Document No. 134:212754 Selective antagonists of A2B adenosine receptors. Biaggioni, Italo O.; Feoktistov, Igor A.; Wells, Jack N. (Vanderbilt University, USA). PCT Int. Appl. WO 2001016134 A1 20010308, 24 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US40751 20000828. PRIORITY: US 1999-PV151649 19990831.

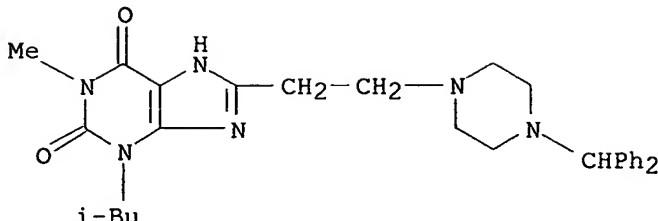
GI



AB Xanthine derivs. of formula I (R = aliph. or cycloaliph. amine) or a pharmaceutically acceptable salt thereof are described as antagonists of A2B adenosine receptors. The compds. are formulated into tablets, aerosols, injections, and suppositories, and may be used to treat various diseases, including asthma and diarrhea.  
 IT 329024-77-3  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (compns. and therapeutic uses of xanthine derivs. as selective antagonists of A2B adenosine receptors)  
 RN 329024-77-3 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3-(2-methylpropyl)-8-(1-pyrrolidinyl)-(9CI) (CA INDEX NAME)



L5 ANSWER 20 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 2001:152520 Document No. 134:202703 Synergistic combination of a phosphodiesterase (PDE) inhibitor and a .beta.2-adrenoceptor agonist for treatment of respiratory tract disorders. Beume, Rolf; Bundschuh, Daniela; Hatzelmann, Armin; Schudt, Christian; Weimar, Christian; Kilian, Ulrich (Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany). PCT Int. Appl. WO 2001013953 A2 20010301, 23 pp. DESIGNATED STATES: W: AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP7852 20000811. PRIORITY: EP 1999-116447 19990821.  
 AB The invention discloses the combined administration of PDE inhibitors and .beta.2-adrenoceptor agonists for the treatment of respiratory tract disorders.  
 IT 90749-32-9, Laprafylline  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (phosphodiesterase inhibitor-.beta.2-adrenoceptor agonist synergistic combination for treatment of respiratory tract disorders)  
 RN 90749-32-9 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)-(9CI) (CA INDEX NAME)



L5 ANSWER 21 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2001:137876 Document No. 134:322242 CoMFA-based comparison of two models of binding site on adenosine A1 receptor. Doytchinova, Irini (Department of Chemistry, Faculty of Pharmacy, Medical University Sofia, Sofia, 1000, Bulg.). Journal of Computer-Aided Molecular Design, 15(1), 29-39 (English) 2001. CODEN: JCAEQ. ISSN: 0920-654X. Publisher: Kluwer Academic Publishers.

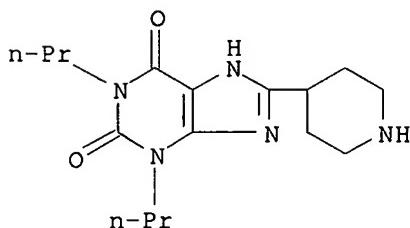
AB A set of 32 N6-substituted adenosines and 22 8-substituted xanthines with affinity for adenosine A1 receptors was subjected to three-dimensional quant. structure-affinity relationship anal. using comparative mol. field anal. (CoMFA). The aim was to compare two modes of binding to the receptor, N6-C8 and N6-N7. Good models with high predictive power and stability were obtained. A comparison of these models gives the following results: (a) Inclusion of both steric and electrostatic fields in CoMFA generates better predictive models compared to models based on steric or electrostatic fields alone. (b) The N6-N7 CoMFA models are slightly better than the N6-C8 ones. (c) Steric restriction exists around the N6-H in the N6-N7 steric field map, which is absent in the N6-C8 steric field map. This report demonstrates that the N6-N7 mode of binding is a further development of the N6-C8 model with a slightly better predictive ability and more accurate steric and electrostatic overlaps between agonists and antagonists.

IT 108653-59-4 337377-56-7

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(binding; CoMFA-based comparison of two models of ligand binding site on adenosine A1 receptor)

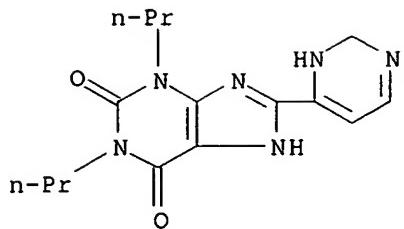
RN 108653-59-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



RN 337377-56-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2,3-dihydro-4-pyrimidinyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



L5 ANSWER 22 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2001:95192 Document No. 134:252191 Reactions of theophyllines. Chemical conversions of 8-aminotheophyllines. Kuz'menko, I. I.; Zvolinskaya, T. V. (Institute of Pharmacology and Toxicology, Ukrainian Academy of Medicinal Sciences, Kiev, 252057, Ukraine). Chemistry of Heterocyclic Compounds (New York) (Translation of Khimiya Geterotsiklicheskih Soedinenii), Volume Date 2000, 36(8), 963-970 (English) 2001. CODEN: CHCCAL. ISSN: 0009-3122. Publisher: Consultants Bureau.

AB Thermally stable, colored 8-aminotheophyllines (betaine derivs. of theophylline) form unstable, colorless salts with strong mineral acids and undergo partial decompr. to a uric acid upon prolonged refluxing with concd. base soln. Substituted 8-pyridinium theophyllines readily take part in typical reactions of the functional group in the substituted pyridine ring with retention of the betaine structure. The formation of the synthesized compds. was confirmed by IR and NMR spectroscopy.

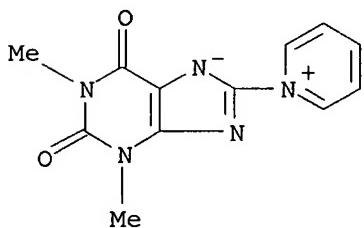
IT 52943-89-2 142954-88-9 142954-89-0

142954-90-3 142954-91-4 199667-06-6

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prep. of betaine derivs. of theophylline)

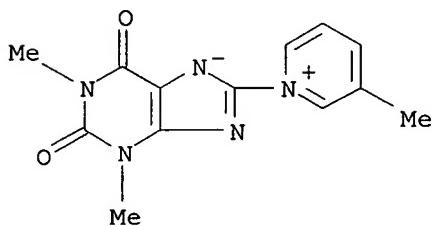
RN 52943-89-2 HCAPLUS

CN Pyridinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)

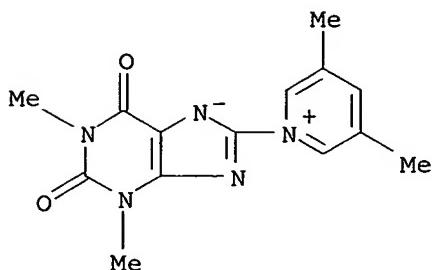


RN 142954-88-9 HCAPLUS

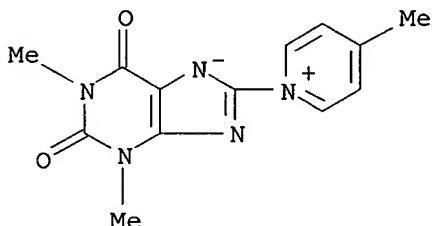
CN Pyridinium, 3-methyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



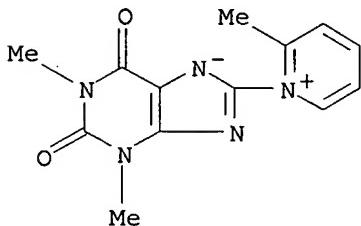
RN 142954-89-0 HCAPLUS  
CN Pyridinium, 3,5-dimethyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



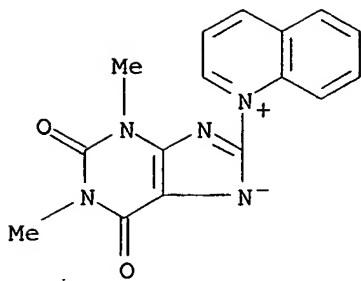
RN 142954-90-3 HCAPLUS  
CN Pyridinium, 4-methyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



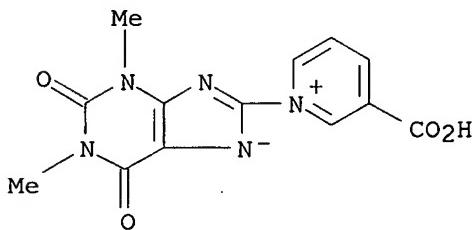
RN 142954-91-4 HCAPLUS  
CN Pyridinium, 2-methyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



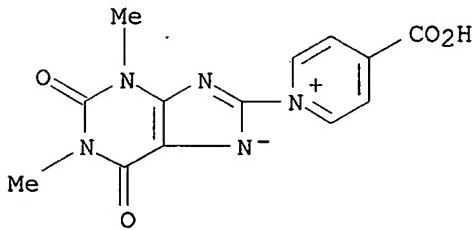
RN 199667-06-6 HCAPLUS  
CN Quinolinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



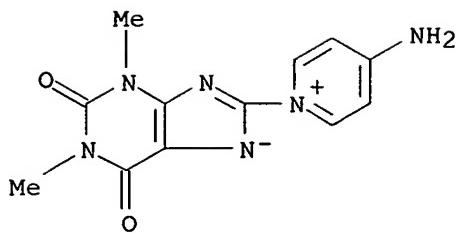
IT 331230-66-1P 331230-67-2P 331230-68-3P  
 331230-69-4P 331230-70-7P 331230-71-8P  
 331230-72-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. of betaine derivs. of theophylline)  
 RN 331230-66-1 HCAPLUS  
 CN Pyridinium, 3-carboxy-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



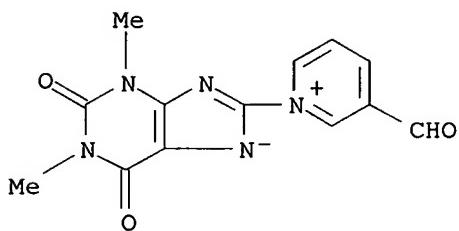
RN 331230-67-2 HCAPLUS  
 CN Pyridinium, 4-carboxy-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



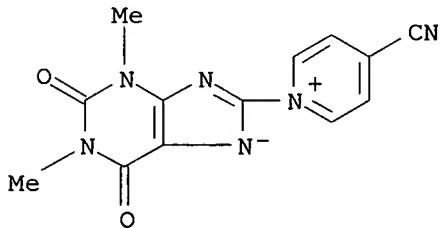
RN 331230-68-3 HCAPLUS  
 CN Pyridinium, 4-amino-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



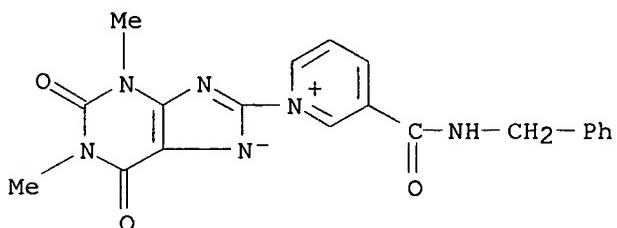
RN 331230-69-4 HCAPLUS  
 CN Pyridinium, 3-formyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



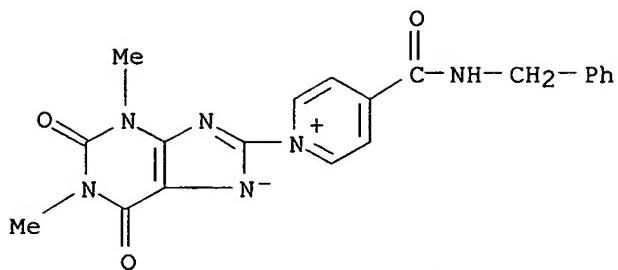
RN 331230-70-7 HCAPLUS  
 CN Pyridinium, 4-cyano-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



RN 331230-71-8 HCAPLUS  
 CN Pyridinium, 3-[(phenylmethyl)amino]carbonyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



RN 331230-72-9 HCAPLUS  
 CN Pyridinium, 4-[(phenylmethyl)amino]carbonyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)

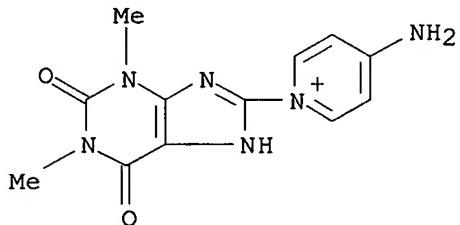


IT 331230-59-2P 331230-60-5P 331230-61-6P  
 331230-62-7P 331230-63-8P 331230-64-9P  
 331230-65-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of betaine derivs. of theophylline)

RN 331230-59-2 HCAPLUS

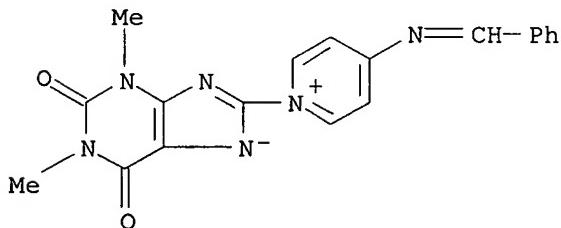
CN Pyridinium, 4-amino-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, chloride (9CI) (CA INDEX NAME)



● Cl<sup>-</sup>

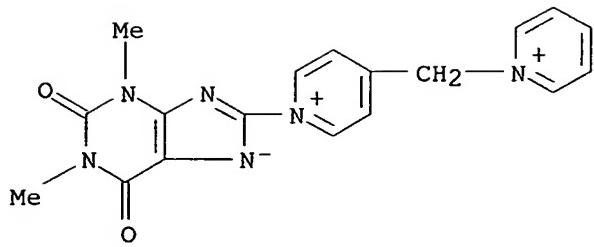
RN 331230-60-5 HCAPLUS

CN Pyridinium, 4-[ (phenylmethylene)amino]-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



RN 331230-61-6 HCAPLUS

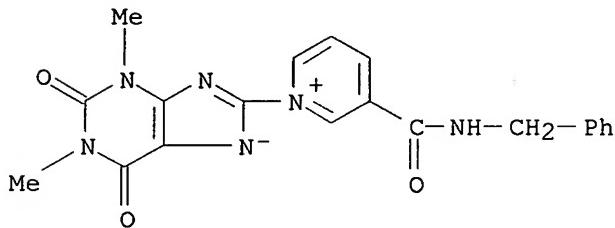
CN Pyridinium, 4-(pyridiniomethyl)-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt, iodide (9CI) (CA INDEX NAME)



● I -

RN 331230-62-7 HCAPLUS

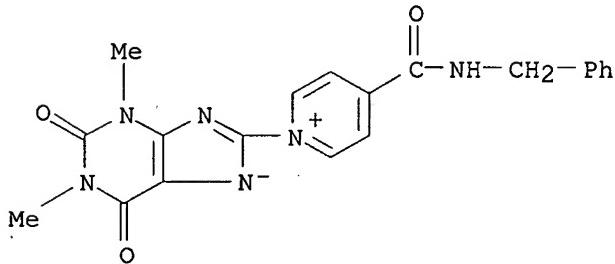
CN Pyridinium, 3-[[ (phenylmethyl)amino]carbonyl]-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt, sodium salt (9CI) (CA INDEX NAME)



● Na

RN 331230-63-8 HCAPLUS

CN Pyridinium, 4-[[ (phenylmethyl)amino]carbonyl]-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt, sodium salt (9CI) (CA INDEX NAME)

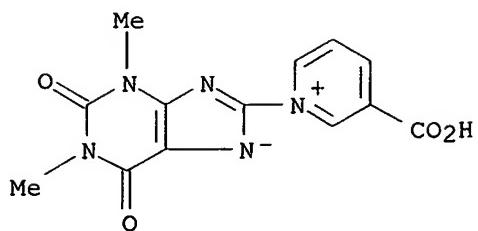


● Na

RN 331230-64-9 HCAPLUS

CN Pyridinium, 3-carboxy-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-

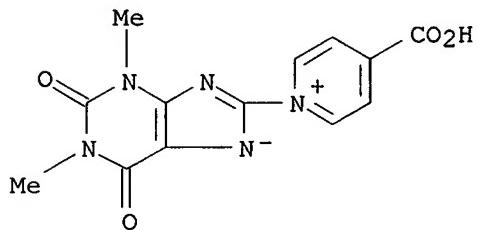
purin-8-yl)-, inner salt, sodium salt (9CI) (CA INDEX NAME)



● Na

RN 331230-65-0 HCPLUS

CN Pyridinium, 4-carboxy-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt, sodium salt (9CI) (CA INDEX NAME)



● Na

L5 ANSWER 23 OF 163 HCPLUS COPYRIGHT 2002 ACS

2000:304316 Document No. 132:318044 Method for improving insulin sensitivity using an adenosine receptor antagonist. Lanoue, Kathryn F.; Crist, George H.; Linden, Joel M. (The Penn State Research Foundation, USA). U.S. US 6060481 A 20000509, 22 pp., Cont.-in-part of U.S. Ser. No. 86,101, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1999-259201 19990301. PRIORITY: US 1998-86101 19980528.

AB The invention relates to methods for improving insulin sensitivity in a patient using one or more A<sub>2B</sub> adenosine receptor antagonists [e.g. 3-n-propylxanthine] are disclosed. These methods stimulate insulin dependent glucose uptake in muscle.

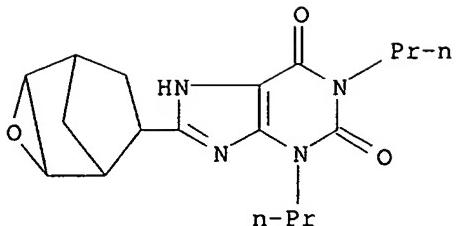
IT 166181-76-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method for improving insulin sensitivity using an adenosine receptor antagonist)

RN 166181-76-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



L5 ANSWER 24 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2000:191630 Document No. 133:68204 CV Therapeutics/Biogen. Flores, Nicholas A. (Imperial College School of Medicine, National Heart and Lung Institute Division, London, W2 1NY, UK). Current Opinion in Cardiovascular, Pulmonary & Renal Investigational Drugs, 2(1), 30-35 (English) 2000. CODEN: CCPRFX. ISSN: 1464-8482. Publisher: PharmaPress Ltd..

AB A review, with 67 refs., of the pharmacol. of CVT-124 (BG-9719), a selective adenosine A1 receptor antagonist under development for the potential treatment of edema assocd. with congestive heart failure, esp. in patients who are resistant to other treatment or who have impaired renal function.

IT 166374-48-7P, CVT 124

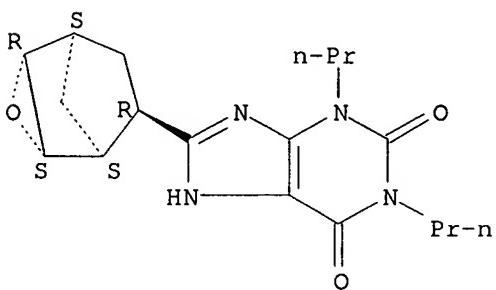
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(pharmacol. of adenosine A1 receptor antagonist CVT-124)

RN 166374-48-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

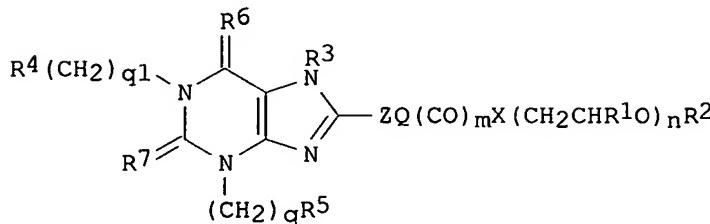


L5 ANSWER 25 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2000:133680 Document No. 132:180589 Preparation of phenylxanthine derivatives as cell adhesion inhibitors.. Daluge, Susan Mary; Jurgensen, Cynthia Holder; Martin, Michael Tolar; Osterhout, Martin Howard (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000009507 A1 20000224, 101 pp.  
 DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,

TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English).  
CODEN: PIXXD2. APPLICATION: WO 1999-EP5814 19990811. PRIORITY: GB  
1998-17623 19980813.

GI



I

AB Title compds. [I; Z = 5-6 membered (substituted) (heteroatom-contg.) cycloalkyl, aryl; R1 = H, Me; R2 = H, alkyl, aryl, aralkyl; m = 0, 1; n = 1-50; X = O, imino, CH2O, CH2NH, etc.; Q = (CH2)p, (CH:CH)p, (C.tplbond.C)p, etc.; R3 = H, (substituted) alkyl, alkenyl, alkynyl, aminoalkyl; R4, R5 = H, cycloalkyl, alkyl, alkenyl, (substituted) aryl, heterocyclyl; R6, R7 = O, S; q, q1 = 0-10; with provisos], were prep'd. Thus, (E)-4-[1,3-bis(benzyl)-1,2,3,6-tetrahydro-2,6-dioxo-9H-purin-8-yl]cinnamic acid (prepn. given) in DMF was heated to near reflux and treated with carbonyldiimidazole followed by stirring for 18 h to give (E)-1,3-bis(benzyl)-8-[3-[2-(1H-imidazol-1-ylcarbonyl)vinyl]phenyl]-9H-purin-2,6(1H,3H)-dione. The latter was refluxed 20 h with nonaethylene glycol monomethyl ether and K2CO3 in MeCN to give 59% (E)-4-[1,3-bis(benzyl)-1,2,3,6-tetrahydro-2,6-dioxo-9H-purin-8-yl]cinnamic acid nonaethylene glycol Me ether ester. I inhibited adhesion of leukocytes to endothelial cell monolayers with IC50's of <0.1 nM to >1000 nM.

IT 259226-39-6P 259226-40-9P

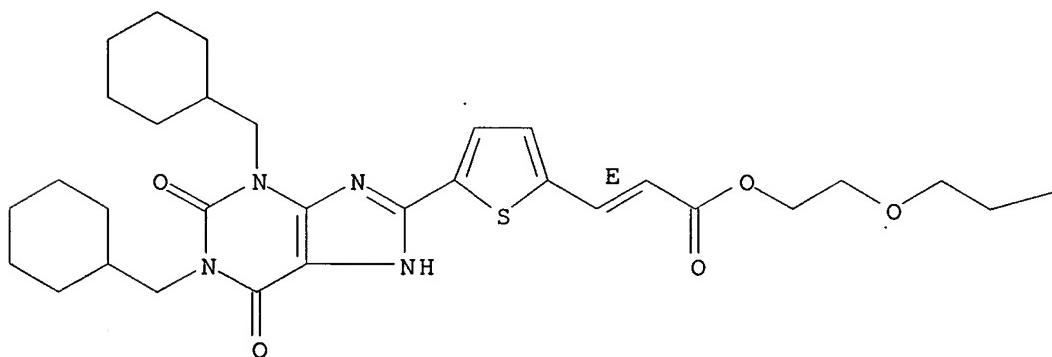
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of phenylxanthine derivs. as cell adhesion inhibitors)

RN 259226-39-6 HCPLUS

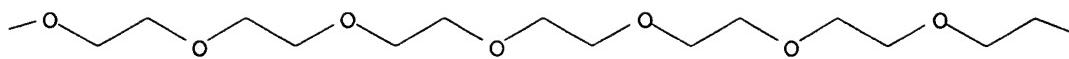
CN 2-Propenoic acid, 3-[5-[1,3-bis(cyclohexylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]-2-thienyl]-, 3,6,9,12,15,18,21,24,27-nonaoxaoctacos-1-yl ester, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

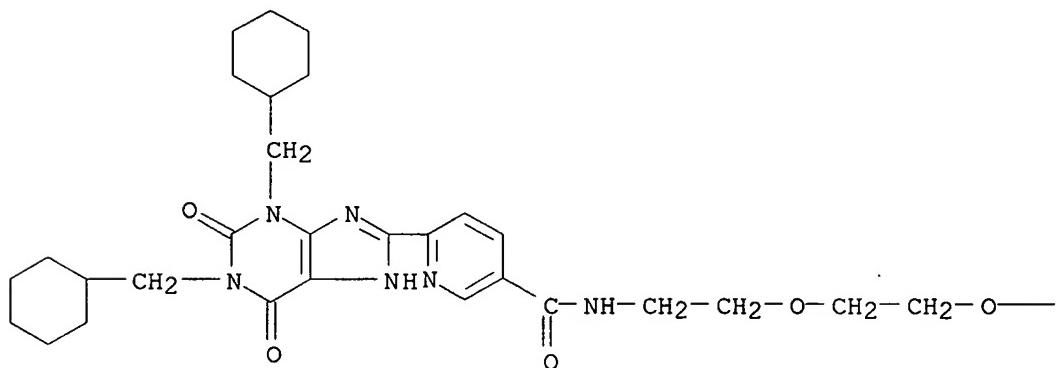


PAGE 1-C

—OMe

RN 259226-40-9 HCAPLUS  
CN 3-Pyridinecarboxamide, 6-[1,3-bis(cyclohexylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]-N-3,6,9,12,15,18,21,24,27-nonaoxaoctacos-1-yl- (9CI)  
(CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— CH<sub>2</sub>— CH<sub>2</sub>— O— CH<sub>2</sub>— CH<sub>2</sub>— O— CH<sub>2</sub>— CH<sub>2</sub>— O— CH<sub>2</sub>— CH<sub>2</sub>— O— CH<sub>2</sub>— CH<sub>2</sub>— O————

PAGE 1-C

— CH<sub>2</sub>— CH<sub>2</sub>— O— CH<sub>2</sub>— CH<sub>2</sub>— OMe

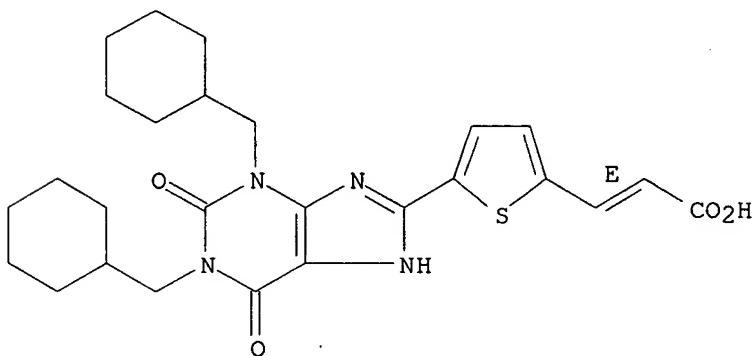
IT   **259226-89-6P 259226-90-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prep. of phenylxanthine derivs. as cell adhesion inhibitors)

RN   259226-89-6   HCAPLUS

CN   2-Propenoic acid, 3-[5-[1,3-bis(cyclohexylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]-2-thienyl]-, (2E)- (9CI)   (CA INDEX NAME)

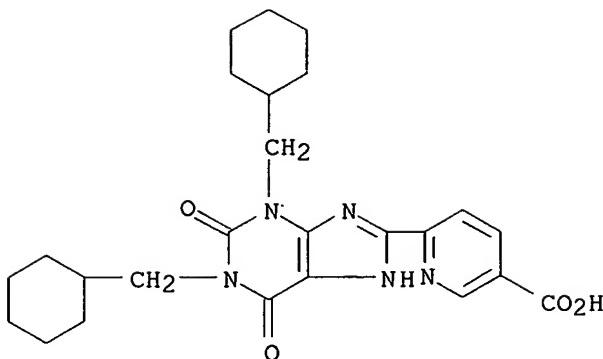
Double bond geometry as shown.



RN   259226-90-9   HCAPLUS

CN   3-Pyridinecarboxylic acid, 6-[1,3-bis(cyclohexylmethyl)-2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl]- (9CI)   (CA INDEX NAME)

Searched by: Mary Hale 308-4258 CM-1 1E01



L5 ANSWER 26 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2000:93325 Document No. 132:102643 Effects of BG9719 (CVT-124), an A<sub>1</sub>-adenosine receptor antagonist, and furosemide on glomerular filtration rate and natriuresis in patients with congestive heart failure. Gottlieb, Stephen S.; Skettino, Sandra L.; Wolff, Andrew; Beckman, Evan; Fisher, Michael L.; Freudenberg, Ronald; Gladwell, Tim; Marshall, Joanne; Cines, Michelle; Bennett, Donald; Liitschwager, Elizabeth B. (Division of Cardiology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA). Journal of the American College of Cardiology, 35(1), 56-59 (English) 2000. CODEN: JACCDI. ISSN: 0735-1097. Publisher: Elsevier Science Inc..

AB To det. the effects of furosemide and the selective A<sub>1</sub> adenosine receptor BG9719 on renal function in patients with congestive heart failure (CHF). Studies suggest that adenosine may affect renal function by various mechanisms, but the effects of blockade of this system in humans is unknown. In addn., the effects of a therapeutic dose of furosemide on glomerular filtration rate (GFR) and renal plasma flow (RPF) in heart failure patients are controversial. On different days, 12 patients received placebo, BG9719 and furosemide. Glomerular filtration rate, RPF and sodium and water excretion were assessed immediately following drug administration. Glomerular filtration rate was 84.+-.23 mL/min/1.73m<sup>2</sup> after receiving placebo, 82.+-.24 following BG9719 administration and a decreased ( $p < 0.005$ ) 63.+-.18 following furosemide. Renal plasma flow was unchanged at 293.+-.124 mL/min/1.73m<sup>2</sup> on placebo, 334.+-.155 after receiving BG9719 and 374.+-.231 after receiving furosemide. Sodium excretion increased from 8.+-.8 mEq following placebo administration to 37.+-.26 mEq following BG9719 administration. In the six patients in whom it was measured, sodium excretion was 104.+-.78 mEq following furosemide administration. Natriuresis is effectively induced by both furosemide and the adenosine A<sub>1</sub> antagonist BG9719 in patients with CHF. Doses of the two drugs used in this study did not cause equiv. sodium and water excretion but only furosemide decreased GFR. These data suggest that adenosine is an important determinant of renal function in patients with heart failure.

IT 166374-48-7, BG9719

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

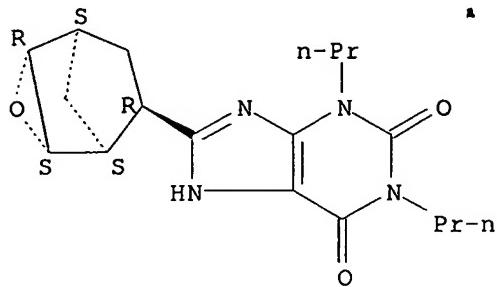
(effects of BG9719 (CVT-124), A<sub>1</sub>-adenosine receptor antagonist, and furosemide on glomerular filtration rate and natriuresis in humans with congestive heart failure)

RN 166374-48-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-

oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 27 OF 163 HCAPLUS COPYRIGHT 2002 ACS

2000:34554 Document No. 132:83673 Combination of loop diuretics with adenosine A1-receptor antagonists for treatment of hypertension and related diseases. Hropot, Max (Kyowa Hakko Kogyo Co., Ltd., Japan). Eur. Pat. Appl. EP 970696 A1 20000112, 10 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1998-108127 19980505.

AB The invention relates to a pharmaceutical compn. contg. combination of a loop diuretic and a adenosine A1 receptor antagonist. This compn. is useful for the treatment of and/or prophylaxis of hypertension, renal failure or disorders with increased proximal tubular reabsorption, e.g., congestive heart failure, liver cirrhosis or nephrotic syndrome. KW-3902 (30 g) was dissolved in a mixed solvent of EtOH (350 g) and CH<sub>2</sub>Cl<sub>2</sub> (350 g), and Eudragit L 100 (90 g) was added to the soln. The resulting soln. was sprayed on the mixt. of furosemide (120 g) and lactose (760 g), and granulated at 60.degree. with a fluidized bed granulator. After drying, the granules were sieved (24 mesh) and mixed uniformly and homogeneously with magnesium stearate in a blender. The resulting granules were filled into hard gelatin capsules. The capsules contg. 5 mg KW-3902 and 20 mg of furosemide were obtained. Results of salidiuretic expts. show that KW-3902 at 0.01 and 0.1 mg/kg and furosemide at 10, 20 and 30 mg/kg body wt. in male Wistar rats orally caused a significant increase in urine vol., sodium and chloride excretion as compared to the control. The combinations of KW-3902 at 0.1 mg/kg with furosemide at 10 mg/kg exerted significant additive or even synergistic effects with respect to urine vol., sodium and chloride excretion in the collection periods 1-4 h as compared with single compds.

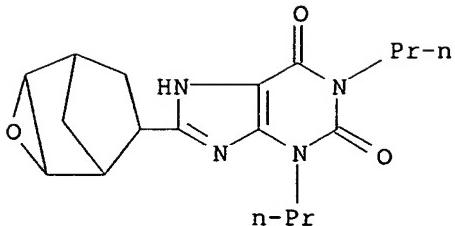
IT 166181-76-6 166374-48-7, CVT-124

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination of loop diuretics with adenosine A1-receptor antagonists for treatment of hypertension and related diseases)

RN 166181-76-6 HCAPLUS

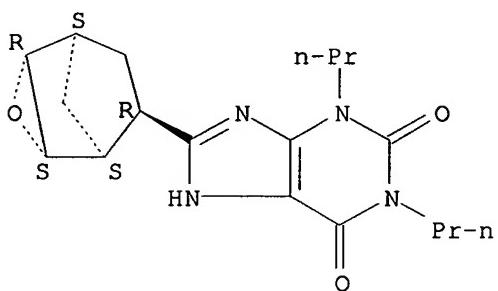
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 166374-48-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 28 OF 163 HCPLUS COPYRIGHT 2002 ACS

2000:9972 Document No. 132:189291 Thermal characterization of some new xanthine derivatives. Danila, G.; Profire, L.; Bumbu, G. G.; Vasile, C. ("Gr.T. Popa" Medicine and Pharmacy University, Iasi, Rom.). Thermochimica Acta, 343(1-2), 69-79 (English) 2000. CODEN: THACAS. ISSN: 0040-6031. Publisher: Elsevier Science B.V..

AB In order to enhance and multiply the pharmacol. properties of theophylline, the 8-substituted-7-[2-hydroxy-3-(4-acetyl-amino)-fenoxy-propyl]-1,3-dimethyl-xanthine derivs. with various substituents have been synthesized. Their chem. structures have been assessed by IR and 1H NMR spectroscopy and elemental anal. The influence of the non-cyclic and cyclic substituents on the thermal and thermo-oxidative behaviors has been followed by thermogravimetry and differential scanning calorimetry. These methods are useful to det. thermal stability, the purity of the compds. and crystallinity. The pharmacol. tests have proved their action both on bronchopulmonary and cardiovascular systems.

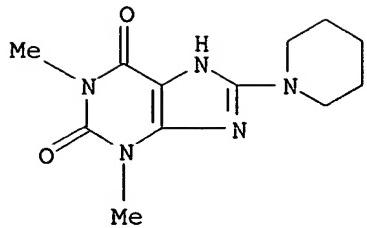
IT 961-48-8 30958-49-7 30958-51-1

145351-66-2 191355-35-8 191355-36-9

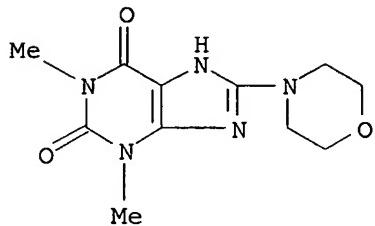
RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis, thermal properties and pharmacol. action of xanthine derivs.)

RN 961-48-8 HCPLUS

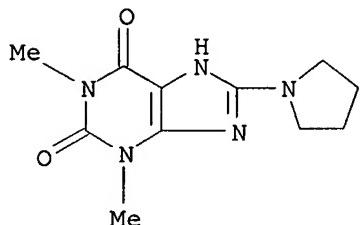
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



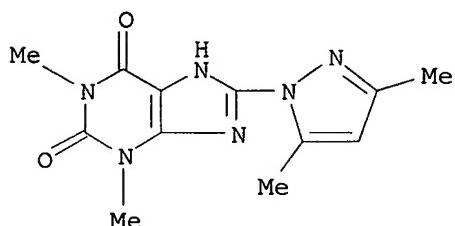
RN 30958-49-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- (9CI)  
(CA INDEX NAME)



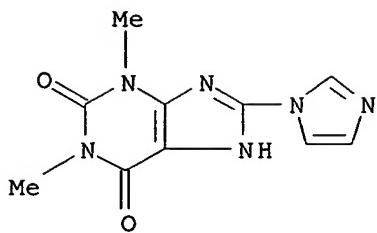
RN 30958-51-1 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-pyrrolidinyl)- (9CI)  
(CA INDEX NAME)



RN 145351-66-2 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-(3,5-dimethyl-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

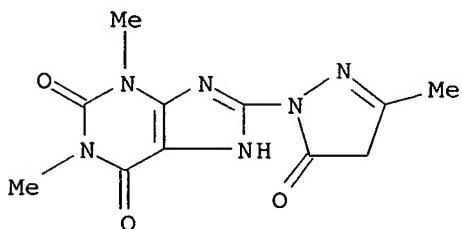


RN 191355-35-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1H-imidazol-1-yl)-1,3-dimethyl- (9CI)  
(CA INDEX NAME)



RN 191355-36-9 HCPLUS

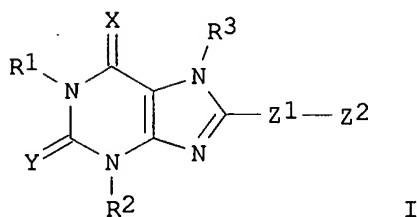
CN 1H-Purine-2,6-dione, 8-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 29 OF 163 HCPLUS COPYRIGHT 2002 ACS

1999:736230 Document No. 131:337033 Immunosuppressive effects of 8-substituted xanthine derivatives. Waer, Mark Jozef Albert; Herdewijn, Piet Andre Maurits Maria; Pfleiderer, Wolfgang (K.U. Leuven Research and Development, Belg.). Eur. Pat. Appl. EP 956855 A1 19991117, 24 pp.  
DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW.  
APPLICATION: EP 1998-201323 19980424.

GI



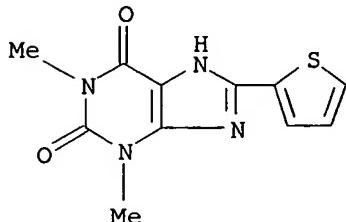
I

AB The title compds. [I; R1-R3 = H, (un)satd. alkyl; X, Y = O, S; Z1 = thienyl, furanyl, cyclopentyl, etc.; Z2 = Ph, sulfonic acid; (un)substituted sulfonamide, etc.], useful for the treatment of auto-immuno disorders, were prepd. Thus, alkylation of xanthine I [R1 = H; R2 = R3 = Me; Z1 = H; X = Y = O] with propargyl bromide afforded I [R1 = HC.tpbond.CCH2; R2 = R3 = Me; Z1 = H; X = Y = O] which showed IC50 of > 200 .mu.M in vitro MLR expt.

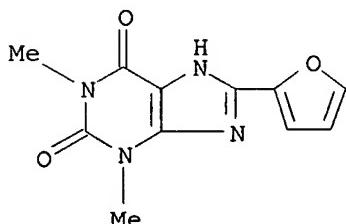
IT 33797-75-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

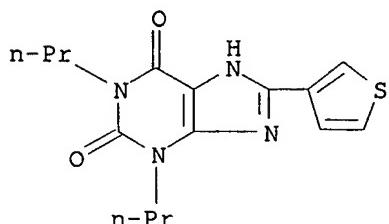
study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(immunosuppressive effects of 8-substituted xanthine derivs.)  
RN 33797-75-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



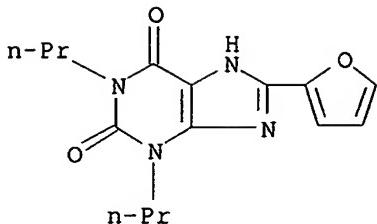
IT 33797-74-9 117027-85-7 117027-86-8  
121542-93-6  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(immunosuppressive effects of 8-substituted xanthine derivs.)  
RN 33797-74-9 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 117027-85-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)

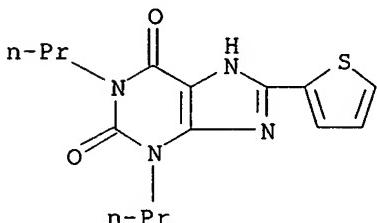


RN 117027-86-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 121542-93-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 30 OF 163 HCPLUS COPYRIGHT 2002 ACS

1999:708611 Document No. 131:317780 Adenosine A1 receptor

antagonist-containing composition and method for restoring diuretic and renal function. Beckman, Evan; Smits, Glenn (Biogen, Inc., USA). PCT Int. Appl. WO 9955339 A1 19991104, 48 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US8879 19990423. PRIORITY: US 1998-83022 19980424; US 1998-83638 19980430.

AB Methods and compns. for restoring diuretic and renal function comprising adenosine A1 antagonists (e.g. BG9719) are provided.

IT 166374-48-7, BG9719 166374-48-7D, BG9719, esters and analogs

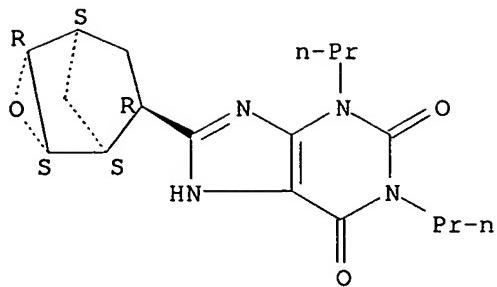
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adenosine A1 antagonist-contg. compn. and method for restoring diuretic and renal function)

RN 166374-48-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

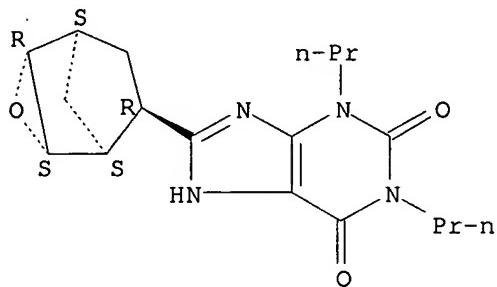
Absolute stereochemistry. Rotation (+).



RN 166374-48-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

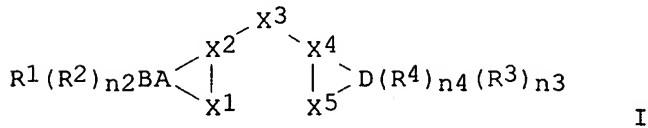


L5 ANSWER 31 OF 163 HCPLUS COPYRIGHT 2002 ACS

1999:354488 Document No. 131:19005 Preparation of

amidinobenzimidazolylheterocycles as anticoagulants.. Fatheree, Paul R.; Jenkins, Thomas E.; Li, Yong; Linsell, Martin S.; Rai, Roopa; Shrader, William D.; Trapp, Sean G.; Young, Wendy B. (Axys Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 9926932 A1 19990603, 105 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US25216 19981125. PRIORITY: US 1997-72654 19971126.

GI



AB Title compds. [I; AB = atoms to form a fused heterobicyclyl; X1, X5 = N, NR5, O, S; R5 = R6, X6R6; X6 = linking group; R6 = H, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, heteropolycycloaryl, polycycloaryl; D =

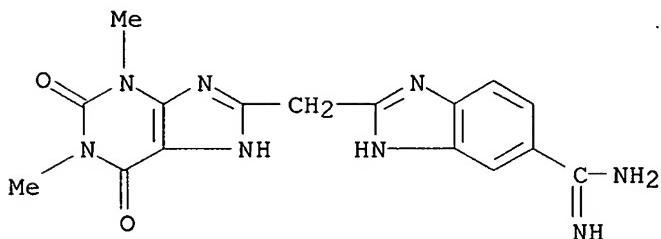
atoms to form a heterocyclyl, heteropolycyclyl; X3 = O, S, CO, NR7, SiR7R8, CR7R8; R7 = H, alkyl, OH; R8 = R6, X6R6; R7 and/or R8 = atoms to form alkylene; R1 = amidino; R2 = H, alkyl, alkoxy, alkylsulfonyl, alkylthio, CO2H, halo, heteroalkyl, OH, SH, NO2; X2, X4 undefined; R3 = H, cyano, halo, NO2, perhaloalkyl, perhaloalkoxy; R4 = R6, X6R6; n2 = 1-3; n3 = 1-4; n4 = 1, 2], were prep'd. Thus, 3,4-diaminobenzamidine, Et 5,6-difluoro-1H-benzimidazol-2-ylacetate, and polyphosphoric acid were heated for 2.5 h at 165.degree. to give 91% 2-(5,6-difluoro-1H-benzimidazol-2-ylmethyl)-1H-benzimidazole-5-carboxamidine. The latter inhibited human Factor Xa with Ki = 0.0008 .mu.M.

IT 226573-50-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of amidinobenzimidazolylheterocycles as anticoagulants)

RN 226573-50-8 HCPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-[(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 32 OF 163 HCPLUS COPYRIGHT 2002 ACS

1999:282101 Document No. 130:306587 Novel use of 8-substituted xanthines for anti-pruritic activity. Griswold, Don E.; Christensen, Siegfried Benjamin Iv (Smithkline Beecham Corporation, USA). PCT Int. Appl. WO 9920280 A1 19990429, 20 pp. DESIGNATED STATES: W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US21886 19981016. PRIORITY: US 1997-63746 19971017.

AB Derivs. of 8-substituted xanthines are used in the prophylactic or therapy of diseases or disorders which have a pruritic component. Rolipram inhibited the pruritus caused by injection of 2 mg/ear arachidonic acid to mice by 75.8%.

IT 132186-73-3 132186-74-4 132186-75-5

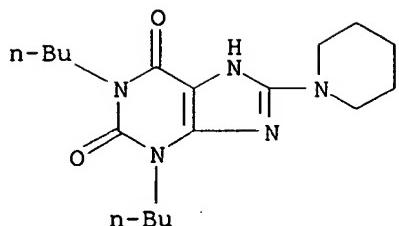
132186-76-6 132186-77-7 132210-44-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(novel use of substituted xanthines for anti-pruritic activity)

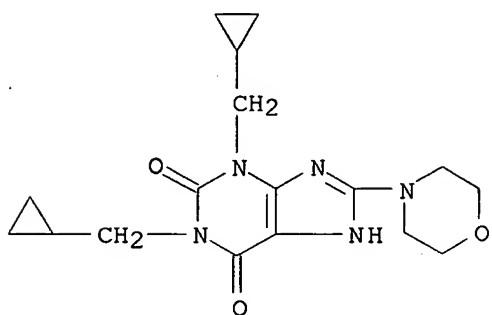
RN 132186-73-3 HCPLUS

CN 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



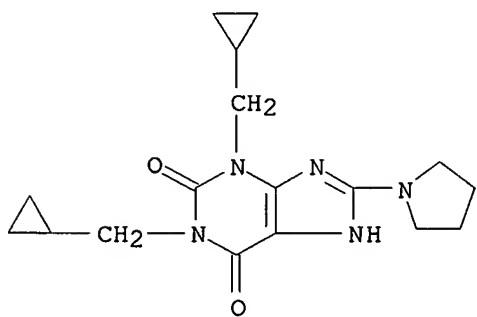
RN 132186-74-4 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(4-morpholinyl)- (9CI) (CA INDEX NAME)



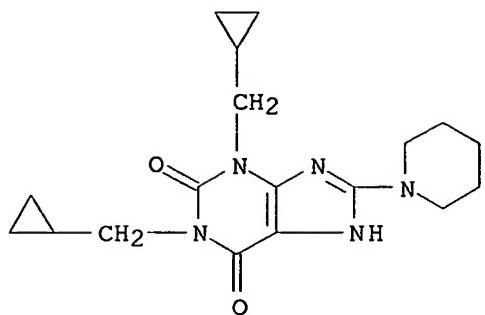
RN 132186-75-5 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

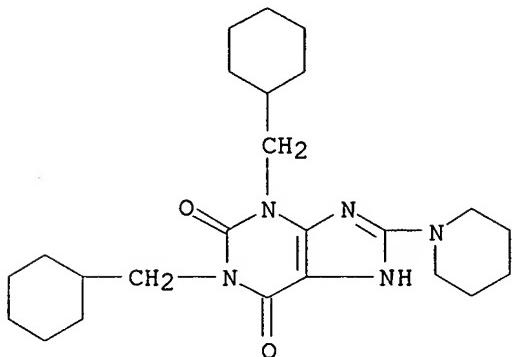


RN 132186-76-6 HCAPLUS

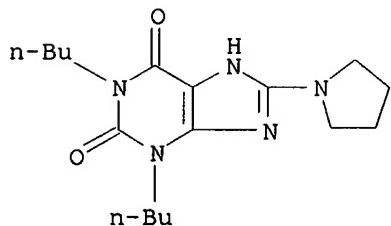
CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



RN 132186-77-7 HCAPLUS  
 CN 1H-Purine-2,6-dione, 1,3-bis(cyclohexylmethyl)-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



RN 132210-44-7 HCAPLUS  
 CN 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-(1-pyrrolidinyl)- (9CI)  
 (CA INDEX NAME)

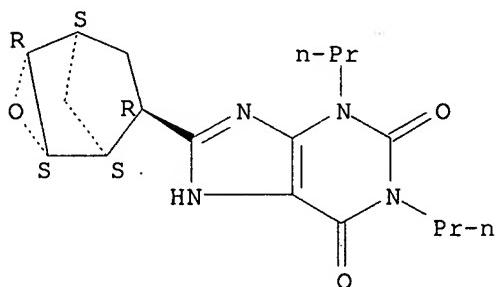


L5 ANSWER 33 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
 1999:239765 Document No. 131:82766 Natriuretic and diuretic actions of a highly selective adenosine A1 receptor antagonist. Wilcox, Christopher S.; Welch, William J.; Schreiner, George F.; Belardinelli, Luiz (Division of Nephrology and Hypertension, Georgetown University Medical Center, Washington, DC, 20007, USA). Journal of the American Society of Nephrology, 10(4), 714-720 (English) 1999. CODEN: JASNEU. ISSN: 1046-6673. Publisher: Lippincott Williams & Wilkins.  
 AB The natriuretic and diuretic action of a highly selective adenosine A1 receptor (A1AdoR) antagonist, 1,3-dipropyl-8-[2-(5,6-

epoxy)norbornyl]xanthine (CVT-124), was investigated in anesthetized rats. CVT-124 (0.1 to 1 mg/kg) caused dose-dependent increases in urine flow and fractional and abs. sodium excretion of by six- to 10-fold and, at 0.1 mg/kg, increased the GFR (1.6.+-.0.1 to 2.5.+-.0.2 mL/min; P < 0.01). There were no changes in BP or heart rate. CVT-124 reduced abs. proximal resorption (26.+-.3 to 20.+-.2 nl/min; P < 0.05) despite unchanged proximally measured, single-nephron GFR (SNGFR) (42.+-.5 to 44.+-.4 nl/min; NS) and thereby decreased fractional proximal resorption (60.+-.3 to 46.+-.4%; P < 0.05). Despite increasing distal tubular fluid flow rate (5.4.+-.0.7 to 9.7.+-.0.9 nl/min; P < 0.001), it reduced the proximal-distal difference in SNGFR (before: 9.4.+-.1.0 vs. during CVT-124: 4.6.+-.1.5 nl/min; P < 0.01), suggesting that it had blunted the effects of the macula densa on SNGFR. Direct measurements of maximal tubuloglomerular feedback (TGF) responses were made from proximal stop flow pressure (PSF) during orthograde loop perfusion from the proximal tubule with artificial tubular fluid at 40 nl/min. TGF was blunted by i.v. CVT-124 (0.5 mg/kg; .DELTA.PSF with vehicle: 8.3.+-.0.6 vs. CVT-124: 6.5.+-.0.3 mmHg; n = 9; P < 0.01). In conclusion, A1AdoR blockade reduces proximal resorption and uncouples it from glomerular filtration. It increases distal delivery of fluid yet does not activate a macula densa-dependent fall in SNGFR because it blunts the TGF response. Natriuresis accompanied by blockade of proximal glomerulotubular balance and TGF characterizes a new class of diuretic drugs.

IT 166374-48-7, CVT-124  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (natriuretic and diuretic actions of a highly selective adenosine A1 receptor antagonist CVT-124)  
 RN 166374-48-7 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

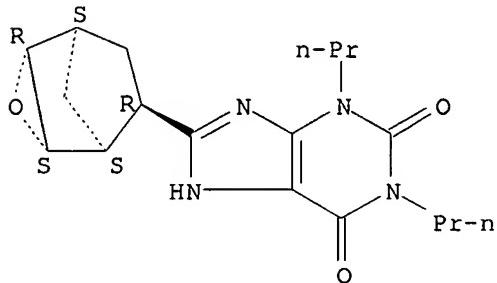


L5 ANSWER 34 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1999:159007 Document No. 130:347121 Renal effects of BG9719, a specific A1 adenosine receptor antagonist, in congestive heart failure. Wolff, Andrew A.; Skettino, Sandra L.; Beckman, Evan; Belardinelli, Luiz (CV Therapeutics, Inc., Palo Alto, CA, 94304, USA). Drug Development Research, 45(3/4), 166-171 (English) 1998. CODEN: DDREDK. ISSN: 0272-4391. Publisher: Wiley-Liss, Inc..  
 AB A1 adenosine receptors mediate renal afferent arteriolar vasoconstriction when distal tubular Na<sup>+</sup> concns. increase (tubuloglomerular feedback, TGF). A1 adenosine receptor stimulation also increases both proximal and distal tubular Na<sup>+</sup> reabsorption. Thus, an A1 adenosine receptor antagonist might produce natriuresis while maintaining renal blood flow and glomerular filtration. BG9719 (also known as CVT-124) is a selective A1 adenosine

receptor antagonist. Its natriuretic properties have been demonstrated both in healthy volunteers and in patients with congestive heart failure (CHF) in double-blind, two-period crossover studies of similar design. In each study, subjects received a single i.v. dose of BG9719 (0.30 mg/kg) or matching placebo on sep. days. BG9719 increased Na<sup>+</sup> excretion in both volunteers and CHF patients; the effects were proportionately greater in CHF. In volunteers, mean Na<sup>+</sup> excretion during the first 3 h after BG9719 was more than double that after placebo (151.5 mEq vs. 63.8 mEq; P < 0.001); whereas in CHF patients, the increase was nearly fourfold (54.5 mEq vs. 15.0 mEq; P < 0.05). In contrast, effects on K<sup>+</sup> excretion were small. In volunteers, mean K<sup>+</sup> excretion was 22.7 mEq on BG9719 vs. 19.3 mEq on placebo (P<0.05); in CHF, these values were 11.8 mEq vs. 7.5 mEq, resp. (P = 0.06). Uric acid was not retained and creatinine clearance was not affected in either group. Mean Cmax was similar in volunteers and CHF patients, but clearance of the drug was reduced in CHF, resulting in a longer half-life. Increases in Na<sup>+</sup> excretion with minimal urinary K<sup>+</sup> losses suggest inhibition of both proximal tubular Na<sup>+</sup> reabsorption and distal Na<sup>+</sup>-K<sup>+</sup> exchange by BG9719. A stable creatinine clearance despite natriuresis is consistent with TGF interruption. These properties may render BG9719 esp. useful in diuretic-resistant patients with CHF complicated by renal dysfunction.

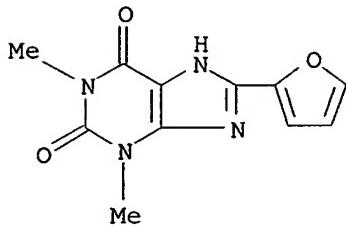
IT 166374-48-7, BG 9719  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (renal effects of epoxynorbornylxanthine deriv. BG9719, a specific A1 adenosine receptor antagonist, in congestive heart failure)  
 RN 166374-48-7 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

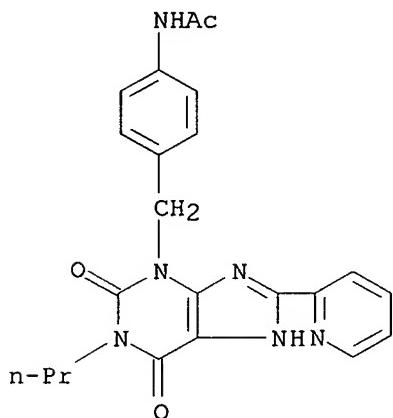


L5 ANSWER 35 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1999:62516 Document No. 130:168156 A mild method for the preparation of 8-substituted xanthines from 5,6-diaminouracils. De Araujo, Aline D.; Bacher, Edmond; Demnitz, F. W. Joachim; Santos, Douglas A. (Departamento de Quimica Fundamental, Universidade Federal de Pernambuco, Recife, CEP 50.670-901, Brazil). Heterocycles, 51(1), 29-36 (English) 1999. CODEN: HTCYAM. ISSN: 0385-5414. OTHER SOURCES: CASREACT 130:168156. Publisher: Japan Institute of Heterocyclic Chemistry.  
 AB The Schiff base derivs. prep'd. from the resp. 5,6-diaminouracil and aldehydes can be mildly oxidatively cyclized with m-CPBA in MeCN to afford C-8 substituted xanthines.  
 IT 33797-74-9P 220419-61-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep'n. of 8-substituted xanthines from 5,6-diaminouracils)

RN 33797-74-9 HCPLUS  
CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 220419-61-4 HCPLUS  
CN Acetamide, N-[4-[(1,2,6,7-tetrahydro-2,6-dioxo-1-propyl-8-(2-pyridinyl)-3H-purin-3-yl)methyl]phenyl]- (9CI) (CA INDEX NAME)

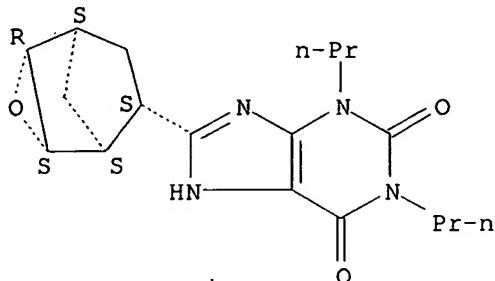


L5 ANSWER 36 OF 163 HCPLUS COPYRIGHT 2002 ACS  
1999:9714 Document No. 130:71627 Compositions and methods for preventing restenosis following revascularization procedures. Martin, Pauline L.; McAfee, Donald A. (Discovery Therapeutics, Inc., USA). PCT Int. Appl. WO 9857651 A1 19981223, 26 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US12717 19980618. PRIORITY: US 1997-50031 19970618.

AB In the present invention, a method is provided which reduces or prevents restenosis following revascularization procedures. It has now been found that selective stimulation of adenosine A<sub>2A</sub> receptors can reduce or prevent such restenosis. This method may be achieved either by: (a) the administration of selective adenosine A<sub>2A</sub> receptor agonists, (b) the administration of a selective adenosine A<sub>1</sub> antagonist in combination with either a selective adenosine A<sub>2A</sub> receptor agonist or a non-selective adenosine agonist, or (c) the administration of a selective adenosine A<sub>1</sub> antagonist in order to block adenosine A<sub>1</sub> receptor activation by endogenously-released adenosine. The present invention is also directed to an improved surgical procedure that relies upon selective stimulation of adenosine A<sub>2A</sub> receptors. The degree of arterial stenosis in rabbits after angioplasty treated with the adenosine A<sub>2A</sub> selective agonist 2-cyclohexylmethylenehydrazinoadenosine was significantly less than

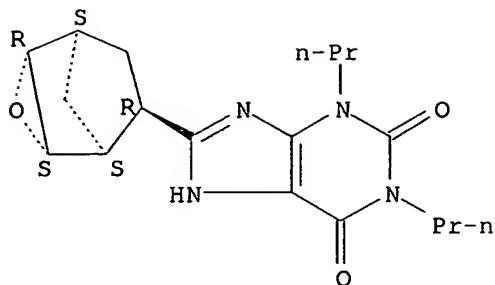
arterial stenosis in rabbits treated with vehicle.  
IT 166374-49-8  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(compsns. for preventing restenosis following revascularization  
procedures)  
RN 166374-49-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6S)-3-  
oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 37 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
1998:625897 Document No. 129:339706 CVT-124, a novel adenosine A1 receptor antagonist with unique diuretic activity. Gellai, Miklos; Schreiner, George F.; Ruffolo, Robert R., Jr.; Fletcher, Tracey; DeWolf, Robin; Brooks, David P. (Department of Renal Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, USA). Journal of Pharmacology and Experimental Therapeutics, 286(3), 1191-1196 (English) 1998. CODEN: JPETAB. ISSN: 0022-3565. Publisher: Williams & Wilkins.  
AB Administration of the selective adenosine A1 receptor antagonist, CVT-124, to conscious chronically instrumented rats resulted in significant increases in urine flow rate and sodium excretion without affecting potassium excretion or renal hemodynamics. Its max. effect was twice that of hydrochlorothiazide which was assocd. with a significant kaliuresis. The diuretic effect of CVT-124 was less than that obsd. with furosemide; however, furosemide administration was assocd. with a large increase in potassium excretion as well as a redn. in glomerular filtration rate. When given at equinatriuretic doses, CVT-124 enhanced the diuretic and natriuretic activity of furosemide without further increasing potassium excretion. In contrast, the combination of hydrochlorothiazide and furosemide resulted in a 3-fold increase in potassium excretion. These data suggest that CVT-124 possesses unique diuretic activity and, as such, it represents a potential new therapeutic in fluid retaining disorders. In addn., its unique mechanism of action suggests that CVT-124 would be effective in otherwise diuretic-resistant patients.  
IT 166374-48-7, CVT 124  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(CVT 124; diuretic activity of CVT-124 and effects on renal hemodynamics and excretion of sodium and potassium)  
RN 166374-48-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-  
oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 38 OF 163 HCPLUS COPYRIGHT 2002 ACS

1998:493732 Document No. 129:131238 Screening method for agents for treatment of eye disorders. Trier, Klaus (Klaus Trier Aps, Den.; Trier, Klaus). PCT Int. Appl. WO 9830900 A2 19980716, 100 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-DK1 19980105. PRIORITY: DK 1997-9 19970106; DK 1997-823 19970707; DK 1997-1383 19971201.

AB A method is provided for identification of substances which are applicable for treatment or prevention of an insufficient longitudinal growth of the eye (hypermetropia) or for treatment or prevention of an excessive longitudinal growth of the eye (myopia); substances identified by the method for treating or preventing conditions related to the longitudinal growth of the eye; substances and mixts. of substances for the prepn. of a pharmaceutical compn. for the treatment or prevention of abnormal growth of the axial length of the eye. The identification involves measuring the effect of the substances on the retinal pigment epithelium of the eye, e.g. by detecting the metabolic effect of the substance on the retinal epithelium, the effect on the standing potential or the effect on the proteoglycans of the scleral tissue of the eye, by way of EOG examn., by way on the size of the so-called c-wave in ERG-recordings, or by the state of the Ca<sup>2+</sup>-channels or on the [3H]-ryanodine receptors of the retinal pigment epithelium.

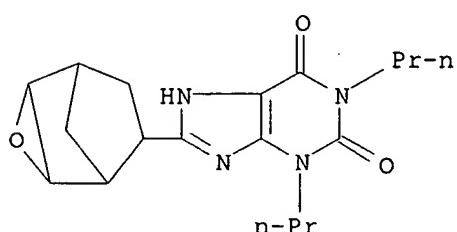
IT 166181-76-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(screening method for agents for treatment of eye disorders)

RN 166181-76-6 HCPLUS

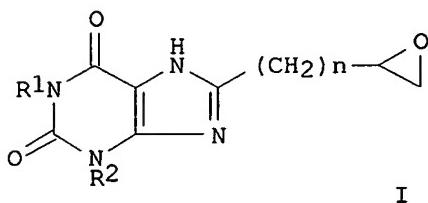
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.0^2,4]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



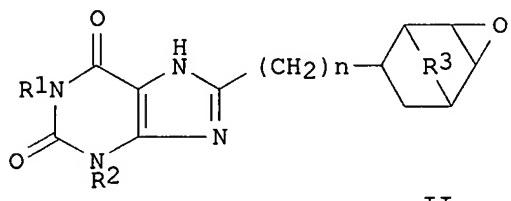
L5 ANSWER 39 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1998:219344 Document No. 128:278988 Xanthine epoxides as A1 adenosine receptor agonists and antagonists, and use for treating cardiac arrhythmias and other disorders. Belardinelli, Luiz; Olsson, Ray; Baker, Stephen; Scammells, Peter J.; Milner, Peter G.; Pfister, Jurg R. (University of Florida Research Foundation, Inc., USA). U.S. US 5736528 A 19980407, 26 pp., Cont.-in-part of U.S. 5,631,260. (English). CODEN: USXXAM. APPLICATION: US 1995-581655 19951229. PRIORITY: US 1993-144459 19931028; US 1994-330640 19941028.

GI



I



II

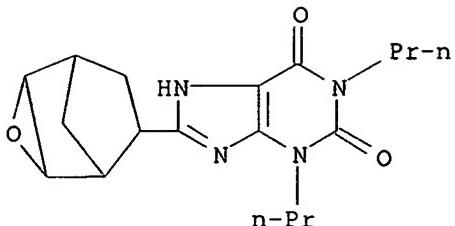
AB N6 -(epoxynorborn-2-yl)adenosines are A1 adenosine receptor agonists that are useful for controlling atrial fibrillation, ventricular rate in atrial flutter, supraventricular tachyarrhythmia, inhibiting A--V- nodal transmission in supraventricular tachycardia, and for normalizing ventricular rhythm and hemodynamics. Xanthine derivs., and compns. comprising those compds., are potent selective antagonists of adenosine receptors. The derivs. and compns. are used to treat conditions, including certain cardiac arrhythmias. The compds., specifically, are C-8 epoxide derivs. of xanthine I (R1, R2 = H, C1-4 alkyl; n = 0-4) and II [R1, R2 = H, C1-4 alkyl; R3 = O, (CH2)1-4; n = 0-4]. Adenosine A1 receptor antagonist activity of 1,3-dipropyl-8-(3-oxatricyclo[3.2.1.02,4]oct-6(7)-yl)-xanthine, and of its R and S enantiomers, is presented. Prepn. of selected derivs., e.g. N6-endo-(3-oxatricyclo[3.2.1.02,4]oct-6(7)-yl)adenosine, is described.

IT 166181-76-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(xanthine epoxides as A1 adenosine receptor agonists and antagonists, and use for treating cardiac arrhythmias and other disorders)

RN 166181-76-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.02,4]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



IT 166374-48-7 190316-06-4

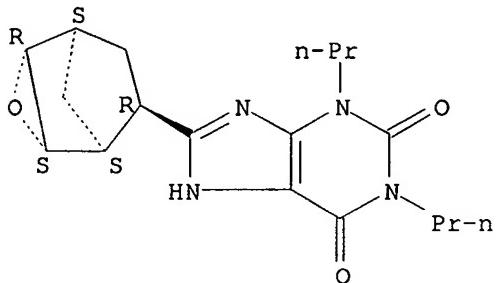
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(xanthine epoxides as A1 adenosine receptor agonists and antagonists, and use for treating cardiac arrhythmias and other disorders)

RN 166374-48-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

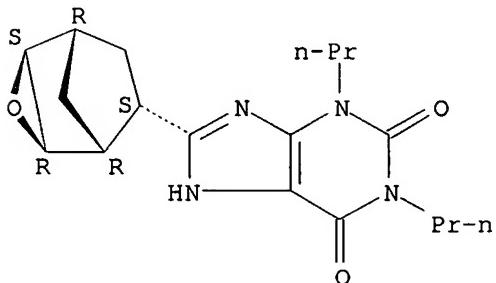
Absolute stereochemistry. Rotation (+).



RN 190316-06-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.02,4]oct-6-yl)-1,3-dipropyl-, [1R-(1.alpha.,2.beta.,4.beta.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



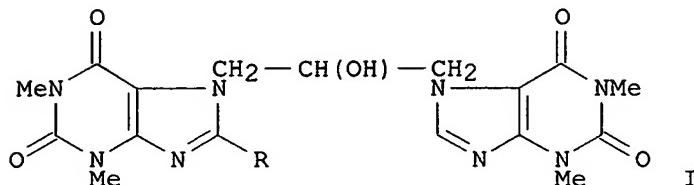
L5 ANSWER 40 OF 163 HCPLUS COPYRIGHT 2002 ACS

1998:123760 Document No. 128:180385 Studies on the methylxanthine series.

IX. Synthesis and physicochemical characterization of 1-(8-substituted 1,3-dimethylxanthin-7-yl)-3-(1,3-dimethylxanthin-7-yl)-2-hydroxypropane derivatives. Profire, Lenuta; Danila, Gh. (Fac. Farmacie, UMF "Gr. T.

Popa, Iasi, Rom.). Farmacia (Bucharest), 45(6), 55-68 (Romanian) 1997.  
CODEN: FRMBAZ. ISSN: 0014-8237. Publisher: Societatea de Stiinte  
Farmaceutice din Romania.

GI

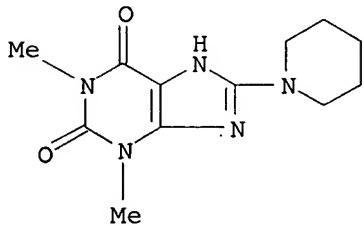


AB Title compds. I (R = H, Br, NO<sub>2</sub>, 1-pyrrolidinyl, piperidino, morpholino, etc.) were prep'd. by reaction of 8-substituted 1,3-dimethylxanthines with 7-(epoxypropyl)-1,3-dimethylxanthine.

IT 961-48-8, 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinyl)- 30958-49-7, 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- 30958-51-1, 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-pyrrolidinyl)- 145351-66-2, 1H-Purine-2,6-dione, 8-(3,5-dimethyl-1H-pyrazol-1-yl)- 3,7-dihydro-1,3-dimethyl- 191355-35-8, 1H-Purine-2,6-dione, 3,7-dihydro-8-(1H-imidazol-1-yl)-1,3-dimethyl- 191355-36-9, 1H-Purine-2,6-dione, 8-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl-  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction with (epoxypropyl)dimethylxanthine)

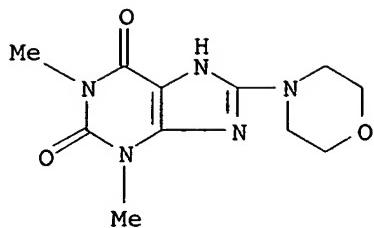
RN 961-48-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinyl)- (9CI)  
(CA INDEX NAME)

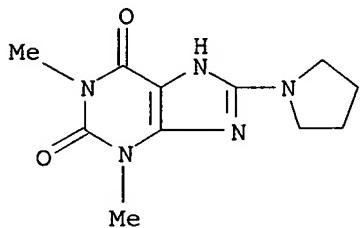


RN 30958-49-7 HCPLUS

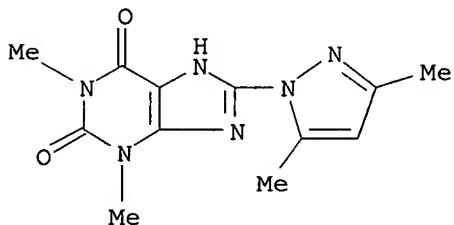
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- (9CI)  
(CA INDEX NAME)



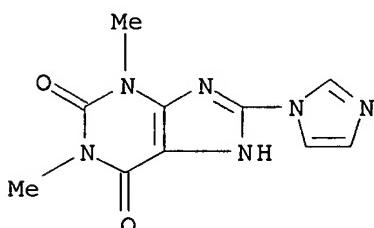
RN 30958-51-1 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-pyrrolidinyl)- (9CI)  
 (CA INDEX NAME)



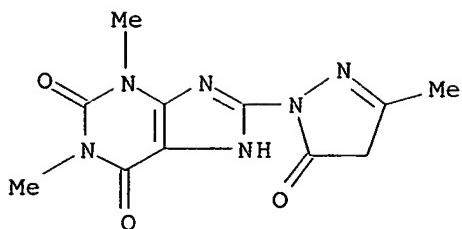
RN 145351-66-2 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-(3,5-dimethyl-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 191355-35-8 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1H-imidazol-1-yl)-1,3-dimethyl- (9CI)  
 (CA INDEX NAME)



RN 191355-36-9 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

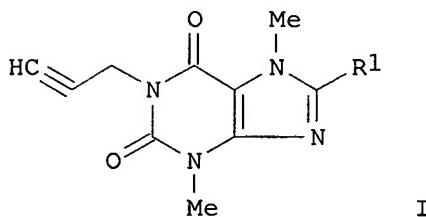


L5 ANSWER 41 OF 163 HCPLUS COPYRIGHT 2002 ACS

1998:31667 Document No. 128:30048 Synthesis and Structure-Activity Relationships of 3,7-Dimethyl-1-propargylxanthine Derivatives, A2A-Selective Adenosine Receptor Antagonists. Mueller, Christa E.; Geis, Uli; Hipp, Jo; Schober, Ulrike; Frobeniu, Wolfram; Pawlowski, Maciej; Suzuki, Fumio; Sandoval-Ramirez, Jesus (Institut fuer Pharmazie und Lebensmittelchemie Pharmazeutische Chemie, Julius-Maximilians-Universitaet Wuerzburg, Wuerzburg, D-97074, Germany). Journal of Medicinal Chemistry, 40(26), 4396-4405 (English) 1997. CODEN: JMCMAR. ISSN: 0022-2623.

Publisher: American Chemical Society.

GI



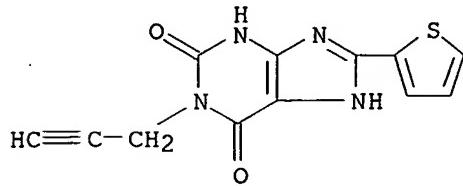
AB A series of 8-substituted derivs. of 3,7-dimethyl-1-propargylxanthine (DMPX), e.g. I (R1 = 3-bromostyryl, 3,4-dimethoxystyryl, 2-thienylethenyl, 2-furylethenyl, etc.) was synthesized and investigated as A2A adenosine receptor antagonists. Different synthetic strategies for the prepn. of DMPX derivs. and analogs were explored. A recently developed synthetic procedure starting from 3-propargyl-5,6-diaminouracil proved to be the method of choice for the prepn. of this type of xanthine derivs. The novel compds. were investigated in radioligand binding studies at the high-affinity adenosine receptor subtypes A1 and A2A and compared with std. A2A adenosine receptor antagonists. Structure-activity relationships were analyzed in detail. 8-Styryl-substituted DMPX derivs. were identified that exhibit high affinity and selectivity for A2A adenosine receptors, including 8-(m-chlorostyryl)-DMPX (CS-DMPX, Ki A2A = 13 nM, 100-fold selective), 8-(m-bromostyryl)-DMPX (BS-DMPX, Ki A2A = 8 nM, 146-fold selective), and 8-(3,4-dimethoxystyryl)-DMPX (Ki A2A = 15 nM, 167-fold selective). These and other novel compds. are superior to the std. A2A adenosine receptor antagonists KF17837 and CSC with respect to A2A affinity and/or selectivity.

IT 199680-52-9P 199680-92-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and structure-activity relationships of xanthine derivs. as A2A-selective adenosine receptor antagonists)

RN 199680-52-9 HCAPLUS

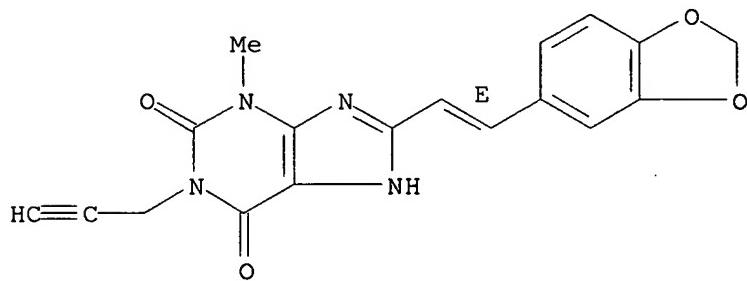
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-(2-propynyl)-8-(2-thienyl)- (9CI) (CA INDEX NAME)



RN 199680-92-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-3,7-dihydro-3-methyl-1-(2-propynyl)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



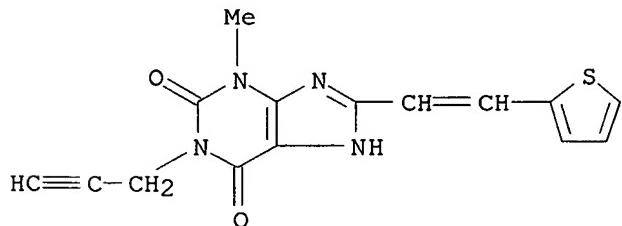
IT 199680-93-8P 199680-94-9P 199680-95-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and structure-activity relationships of xanthine derivs. as A2A-selective adenosine receptor antagonists)

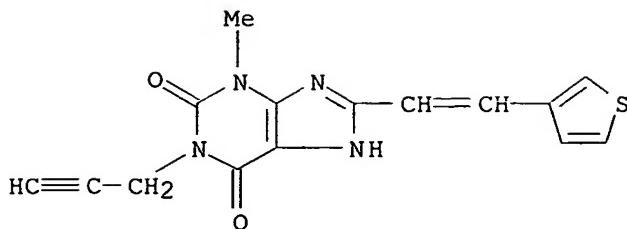
RN 199680-93-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-(2-propynyl)-8-[2-(2-thienyl)ethenyl]- (9CI) (CA INDEX NAME)



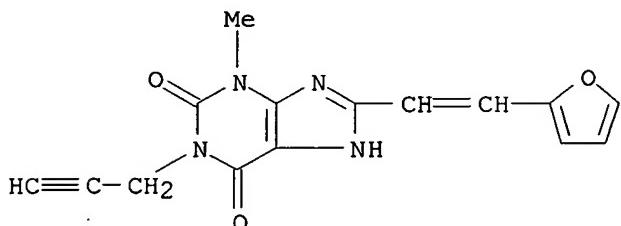
RN 199680-94-9 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-(2-propynyl)-8-[2-(3-thienyl)ethenyl]- (9CI) (CA INDEX NAME)



RN 199680-95-0 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(2-furanyl)ethenyl]-3,7-dihydro-3-methyl-1-(2-propynyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 42 OF 163 HCPLUS COPYRIGHT 2002 ACS

1997:747699 Document No. 128:34732 Betaine derivatives of theophylline: 8-quinoliniotheophyllinate. Zvoliskay, T. V.; Kuzmenko, I. I. (Inst. Farmakol. Toksikol., AMN Ukr., Ukraine). Farmatsevtichni Zhurnal (Kiev) (2), 82-84 (Ukrainian) 1997. CODEN: FRZKAP. ISSN: 0367-3057. Publisher: Zdorov'ya.

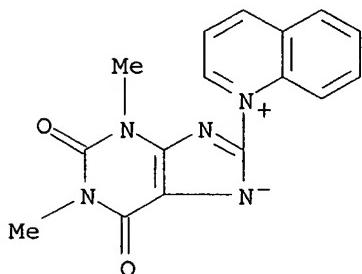
AB The title compd. was prep'd. from 8-chloro- or 8-bromotheophylline and quinoline in the presence of Ac<sub>2</sub>O. Its toxicity and antitumor activity were studied.

IT 199667-06-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn., toxicity and antitumor activity of)

RN 199667-06-6 HCPLUS

CN Quinolinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)

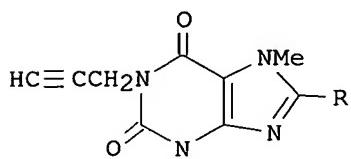


L5 ANSWER 43 OF 163 HCPLUS COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 1E01

1997:644170 Document No. 127:293058 Configurationally stable analogs of styrylxanthines as A2A adenosine receptor antagonists. Muller, C. E.; Schobert, U.; Hipp, J.; Geis, U.; Frobenius, W.; Pawlowski, M. (Pharmazeutische Chemie, Institut Pharmazie und Lebensmittelchemie, Julius-Maximilians-Universitat Wurzburg, Wurzburg, D-97074, Germany). European Journal of Medicinal Chemistry, 32(9), 709-719 (English) 1997. CODEN: EJMCA5. ISSN: 0223-5234. Publisher: Elsevier.

GI



I

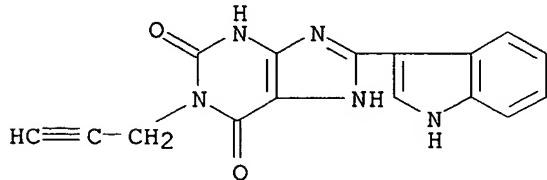
AB Configurationally stable analogs of the potent, a2A-selective adenosine receptor (AR) antagonist 3,7-dimethyl-1-propargyl-8-styrylxanthine (I; R = CH:CHPh) were synthesized and investigated in radioligand binding assays for affinity to the high-affinity A1- and A2A-AR subtypes of rat brain. All derivs. prep'd., including compds. in which the styryl double bond was replaced by a cyclopropane ring or a triple bond, or in which it was integrated into a (hetero) cyclic ring system, were less potent and less selective compared to the parent compd. I (R = CH:CHPh). The best compd. of the present series was 8-(phenylethyynyl)-DMPX (I; R = C.tplbond.CPh), exhibiting a Ki value at A2A-AR of 300 nM and a > 10-fold selectivity vs. A1-AR. In view of its configurational stability, I (R = C.tplbond.CPh), may be an interesting lead compd. for the development of more potent A2A antagonists by introducing appropriate substituents in the Ph ring. Based on conformational anal. of 8-styrylxanthine and 8-(2-naphthyl)xanthine derivs., it is hypothesized that the bioactive conformation of (E)-8-styryl substituents with regard to the imidazole ring of the xanthine nucleus at A2A-AR may be nearly coplanar and cisoid, and may differ from the bioactive conformation of such xanthine derivs. at A1-AR.

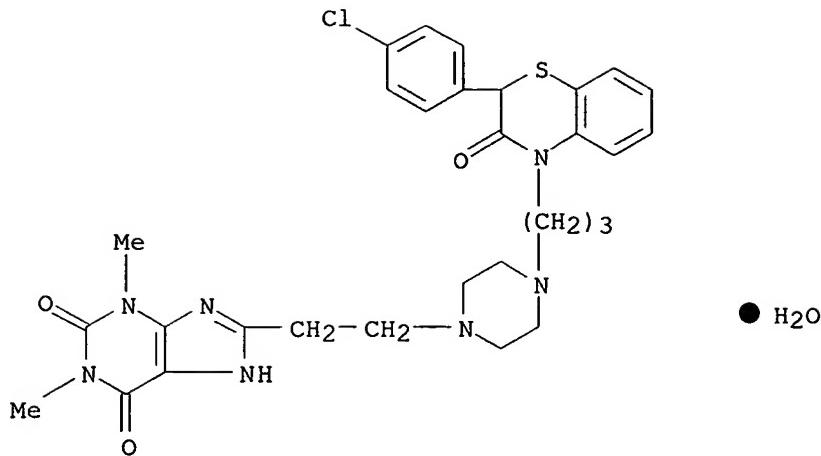
IT 197076-04-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of configurationally stable analogs of styrylxanthines as A2A adenosine receptor antagonists)

RN 197076-04-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1H-indol-3-yl)-1-(2-propynyl)- (9CI)  
(CA INDEX NAME)





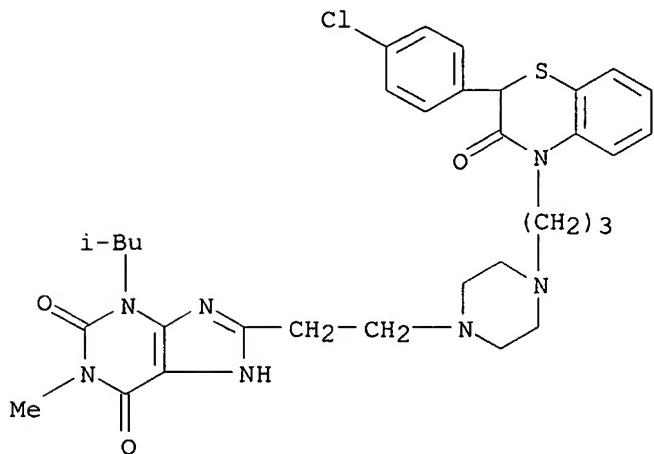
RN 194426-31-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-[3-[2-(4-chlorophenyl)-2,3-dihydro-3-oxo-4H-1,4-benzothiazin-4-yl]propyl]-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)-, ethanedioate (1:1), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 194426-30-7

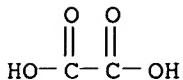
CMF C33 H40 Cl N7 O3 S



CM 2

CRN 144-62-7

CMF C2 H2 O4



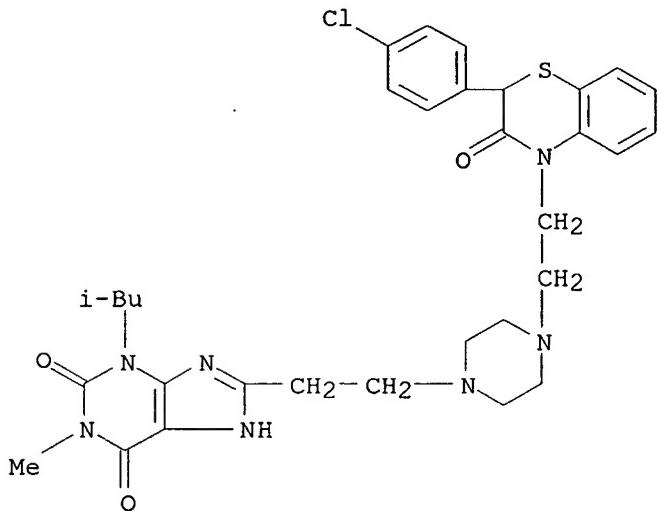
RN 194426-34-1 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-[2-[2-(4-chlorophenyl)-2,3-dihydro-3-oxo-4H-1,4-benzothiazin-4-yl]ethyl]-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)-, ethanedioate (1:1), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 194426-33-0

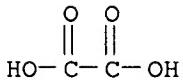
CMF C32 H38 Cl N7 O3 S



CM 2

CRN 144-62-7

CMF C2 H2 O4



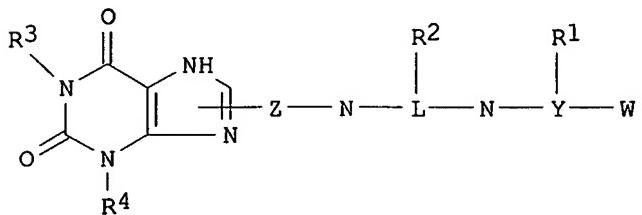
L5 ANSWER 45 OF 163 HCPLUS COPYRIGHT 2002 ACS

1997:543469 Document No. 127:149350 Preparation of nucleosides as adenosine A receptor agonists and antagonists. Belardinelli, Luiz; Olsson, Ray; Baker, Stephen; Scammells, Peter J.; Milner, Peter G.; Pfister, Jurg R. (University of Florida, USA). PCT Int. Appl. WO 9724363 A1 19970710, 63 pp. DESIGNATED STATES: W: AU, BR, CA, CN, JP, KR, MX, NZ; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US20840 19961226. PRIORITY: US 1995-581655 19951229.

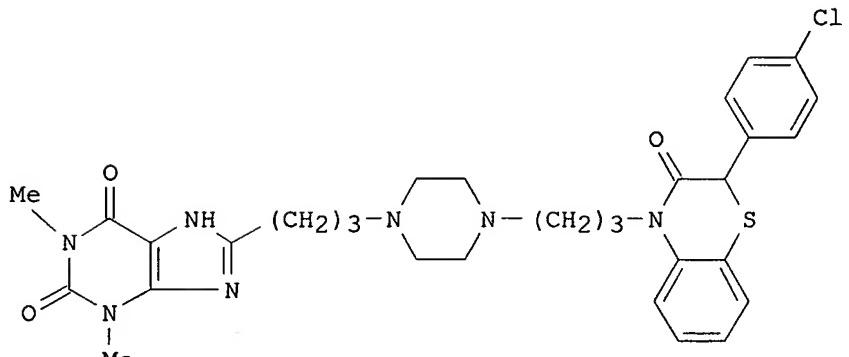
GI

1997:587158 Document No. 127:190751 Preparation of xanthin derivatives as necrosis factor inhibitors. Sugiura, Masaki; Sugita, Naohisa; Sakurai, Hiroaki; Ozeki, Masakatsu; Kotado, Shinichi (Tanabe Seiyaku Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 09227561 A2 19970902 Heisei, 17 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1996-33297 19960221.

GI



I



II

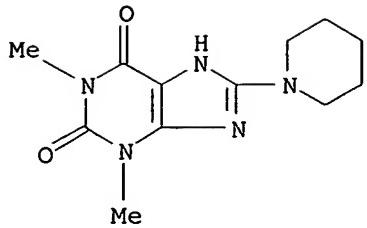
AB The title compds. (I; W = N-contg. heterocycll; Y = single bond, lower alkylene, alkenylene, or alkynylene having CO optionally; Z = lower alkylene, alkenylene, or alkynylene having CO optionally; L = lower alkylene; R1, R2 = H, lower alkyl, etc.; R3, R4 = H, lower alkyl, alkenyl, alkynyl, aryl, etc.) are prep'd. I, possessing tumor necrosis factor inhibitory (NFkB) activity, are useful for prevention and treatment of inflammatory, virus, and autoimmunity diseases. Thus, 2-(4-chlorophenyl)-4-(3-piperazinopropyl)-2,3-dihydro-1,4-benzothiazin-3-one (prepn. given) was reacted with 1,3-dimethyl-8-(3-bromopropyl)xanthin to give 73% the title compd. (II). I were tested and showed inhibitory activity against luciferase.

IT 194426-27-2P 194426-31-8P 194426-34-1P

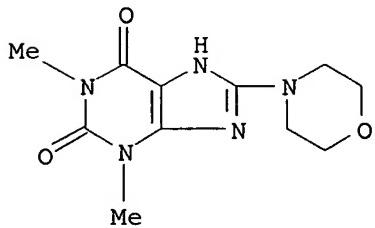
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of xanthin derivs. as necrosis factor inhibitors)

RN 194426-27-2 HCAPLUS

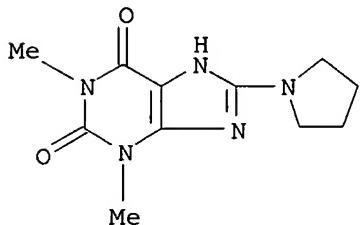
CN 1H-Purine-2,6-dione, 8-[2-[4-[3-[2-(4-chlorophenyl)-2,3-dihydro-3-oxo-4H-1,4-benzothiazin-4-yl]propyl]-1-piperazinyl]ethyl]-3,7-dihydro-1,3-dimethyl-, dihydrochloride, monohydrate (9CI) (CA INDEX NAME)



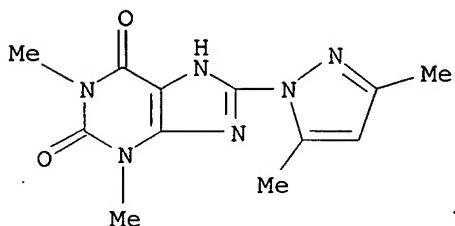
RN 30958-49-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- (9CI)  
(CA INDEX NAME)



RN 30958-51-1 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-pyrrolidinyl)- (9CI)  
(CA INDEX NAME)



RN 145351-66-2 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-(3,5-dimethyl-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 191355-35-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1H-imidazol-1-yl)-1,3-dimethyl- (9CI)  
(CA INDEX NAME)

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

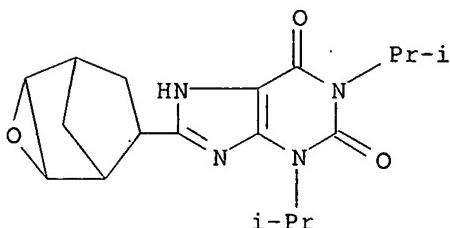
AB Adenosine and xanthine nucleosides I ( $R = R_1, R_2; R_3 =$  alkyl of 1-4 carbons) were prepd. as agonists and antagonists of adenosine A receptors. The derivs. and compns. are used to treat conditions, including certain cardiac arrhythmias. Thus, N6-(exo-5,6-epoxynorborn-2-yl) adenosine was prepd. and inhibited (-)-isoproterenol-simulated cAMP accumulation ( $EC_{50} = 1.1 \text{ } \mu\text{M}$ ,  $0.2 \text{ nM}$ ).

IT 193276-99-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of nucleosides as adenosine a receptor agonists and antagonists)

RN 193276-99-2 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-bis(1-methylethyl)-8-(3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl)- (9CI) (CA INDEX NAME)



L5 ANSWER 46 OF 163 HCPLUS COPYRIGHT 2002 ACS

1997:381630 Document No. 127:65736 Studies on the methylxanthine series.

VIII. Synthesis and physicochemical characterization of some 7-[.beta.-hydroxy-.gamma.- (p-acetamidophenoxy)propyl]-8-R-1,3-dimethylxanthine derivatives. Danila, Gh.; Profire, Lenuta (Fac. farmacie, Iasi, Rom.). Farmacia (Bucharest), 45(1), 45-54 (Romanian) 1997. CODEN: FRMBAZ. ISSN: 0014-8237. Publisher: Societatea de Stiinte Farmaceutice din Romania.

AB The work to the synthesis of some new dyphylline derivs., substituted on C8 and etherified on hydroxyl group. The compds. were synthesized by reaction 1,3-dimethyl-8-R-xanthines with 4-(2,3-epoxypropoxy)acetanilide. We established the working conditions necessary in order to obtain some pure products with better efficiency. The new compds. were characterized by IR and elemental anal.

IT 961-48-8 30958-49-7 30958-51-1

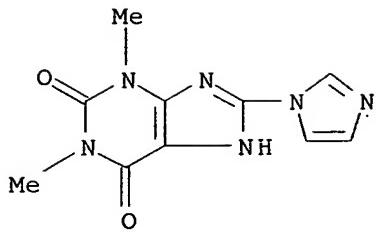
145351-66-2 191355-35-8 191355-36-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(Studies on the methylxanthine series. VIII. Synthesis and physicochem. characterization of some 7-[.beta.-hydroxy-.gamma.- (p-acetamidophenoxy)propyl]-8-R-1,3-dimethylxanthine derivs.)

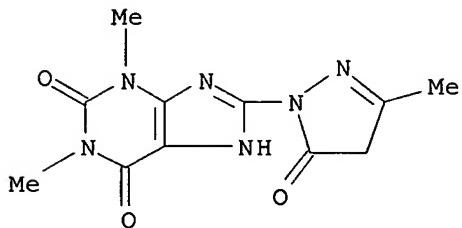
RN 961-48-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



RN 191355-36-9 HCPLUS

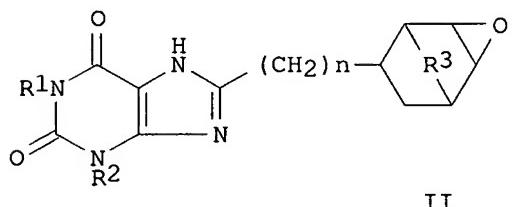
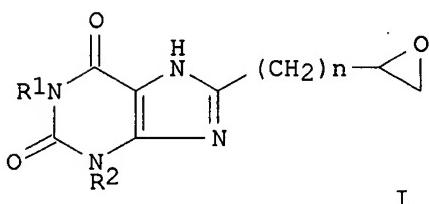
CN 1H-Purine-2,6-dione, 8-(4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 47 OF 163 HCPLUS COPYRIGHT 2002 ACS

1997:342741 Document No. 127:44966 Xanthine epoxides as A1 adenosine receptor agonists and antagonists, and use for treating cardiac arrhythmias and other disorders. Belardinelli, Luiz; Olsson, Ray; Baker, Stephen; Scammells, Peter J.; Milner, Peter G.; Pfister, Jurg R.; Schreiner, George F. (University of Florida Research Foundation, Inc., USA). U.S. US 5631260 A 19970520, 21 pp., Cont.-in-part of U.S. 5,446,046. (English). CODEN: USXXAM. APPLICATION: US 1994-330640 19941028. PRIORITY: US 1993-144459 19931028.

GI



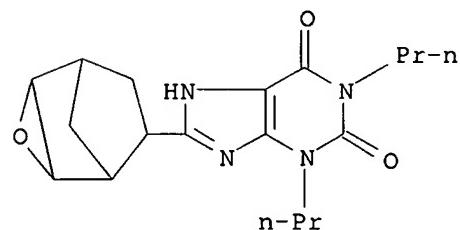
AB Xanthine derivs., and compns. comprising those compds., are potent selective antagonists of adenosine receptors. The derivs. and compns. are used to treat conditions, including certain cardiac arrhythmias. The compds., specifically, are C-8 epoxide derivs. of xanthine I (R1, R2 = H, C1-4 alkyl; n = 0-4) and II [R1, R2 = H, C1-4 alkyl; R3 = O, (CH2)1-4; n = 0-4]. Adenosine A1 receptor antagonist activity of 1,3-dipropyl-8-(3-oxatricyclo[3.2.1.02,4]oct-6(7)-yl)-xanthine, and of its R and S enantiomers, is presented. Prepn. of selected derivs., e.g. N6-endo-(3-oxatricyclo[3.2.1.02,4]oct-6(7)-yl)adenosine, is described.

IT 166181-76-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(xanthine epoxides as A1 adenosine receptor agonists and antagonists, and use for treating cardiac arrhythmias and other disorders)

RN 166181-76-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.02,4]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



IT 166374-48-7 190316-06-4

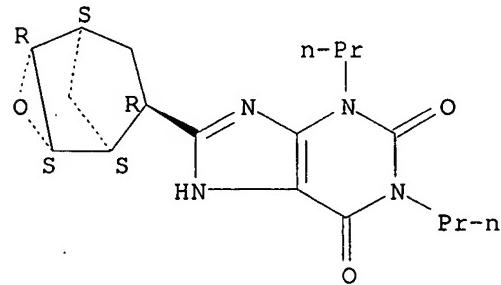
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(xanthine epoxides as A1 adenosine receptor agonists and antagonists, and use for treating cardiac arrhythmias and other disorders)

RN 166374-48-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

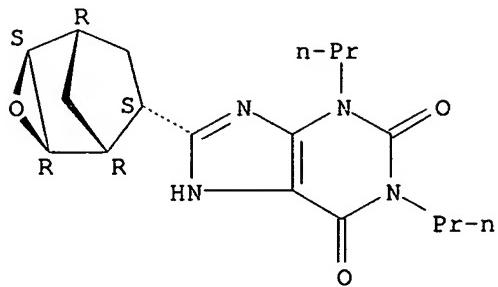
Absolute stereochemistry. Rotation (+).



RN 190316-06-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.02,4]oct-6-yl)-1,3-dipropyl-, [1R-(1.alpha.,2.beta.,4.beta.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

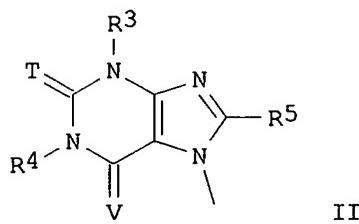
Absolute stereochemistry. Rotation (-).



L5 ANSWER 48 OF 163 HCPLUS COPYRIGHT 2002 ACS

1997:331961 Document No. 126:305588 Preparation of 4-(dioxopurinylmethyl)phenylacetates and analogs as hypolipemics. Connell, Richard; Goldmann, Siegfried; Mueller, Ulrich; Lohmer, Stefan; Bischoff, Hilmar; Denzer, Dirk; Gruetzmann, Rudi; Wohlfeil, Stefan (Bayer A.-G., Germany). Eur. Pat. Appl. EP 764647 A1 19970326, 69 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (German). CODEN: EPXXDW. APPLICATION: EP 1996-114577 19960912. PRIORITY: DE 1995-19535504 19950925.

GI



AB RCH<sub>2</sub>ZCHR<sub>1</sub>C(:L)R<sub>2</sub> [I; R = xanthine moiety, e.g., II; R<sub>1</sub> = H, (cyclo)alkyl, Ph, heterocyclyl, etc.; R<sub>2</sub> = OH, SH, alkoxy, (di)alkylamino, etc.; R<sub>3</sub>, R<sub>4</sub> = H, alkyl, aryl, etc.; R<sub>5</sub> = H, halo, alkyl, aryl, etc.; L, T, V = O or S; Z = (un)substituted 1,4-phenylene] were prepd. Thus, 5,6-diamino-1,3-dimethyluracil was cyclocondensed with 4-MeC<sub>6</sub>H<sub>4</sub>CHO and the product N-alkylated by 4-(BrCH<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>CHR<sub>1</sub>CO<sub>2</sub>CMe<sub>3</sub> (R<sub>1</sub> = cyclopentyl) (prepn. given) to give 4-(RCH<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>CHR<sub>1</sub>CO<sub>2</sub>CMe<sub>3</sub> (R = II, R<sub>1</sub> = cyclopentyl, R<sub>3</sub> = R<sub>4</sub> = Me, R<sub>5</sub> = C<sub>6</sub>H<sub>4</sub>Me-4, T = V = O). Data for biol. activity of I were given.

IT 1029-62-5P 1088-64-8P 1088-65-9P

7145-52-0P 33797-75-0P 93215-03-3P

121542-92-5P 189215-21-2P 189215-22-3P

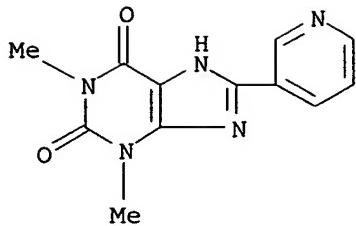
189215-36-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

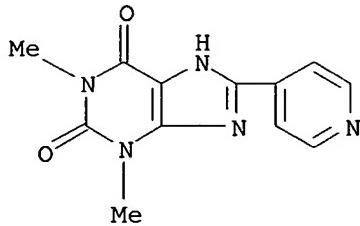
(prepn. of 4-(dioxopurinylmethyl)phenylacetates and analogs as hypolipemics)

RN 1029-62-5 HCPLUS

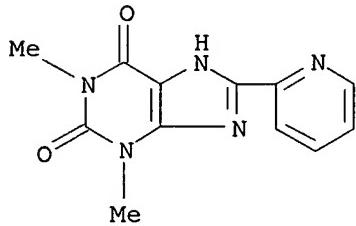
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



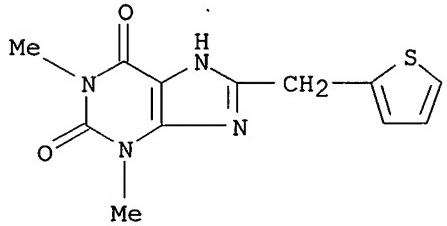
RN 1088-64-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



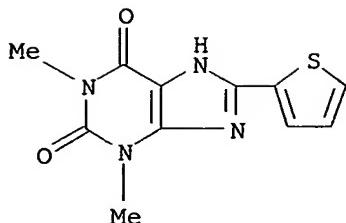
RN 1088-65-9 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-pyridinyl)- (9CI) (CA INDEX NAME)



RN 7145-52-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienylmethyl)- (9CI) (CA INDEX NAME)

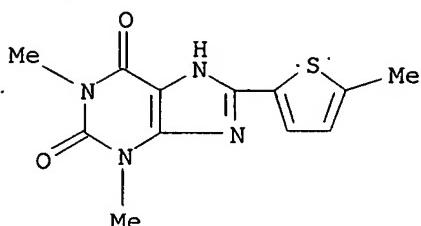


RN 33797-75-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



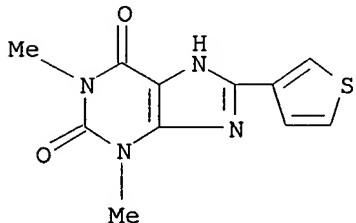
RN 93215-03-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(5-methyl-2-thienyl)- (9CI) (CA INDEX NAME)



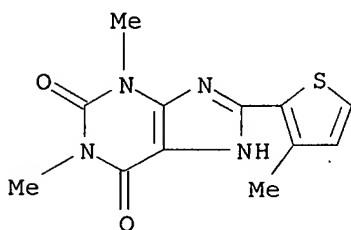
RN 121542-92-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



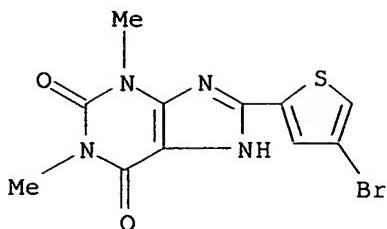
RN 189215-21-2 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-methyl-2-thienyl)- (9CI) (CA INDEX NAME)



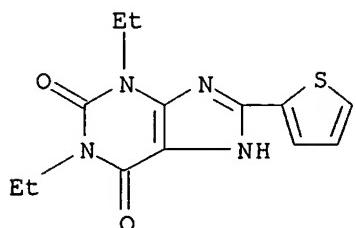
RN 189215-22-3 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(4-bromo-2-thienyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 189215-36-9 HCPLUS

CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-(2-thienyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 49 OF 163 HCPLUS COPYRIGHT 2002 ACS

1997:318284 Document No. 127:260 Synthesis and Biological Evaluation of the Enantiomers of the Potent and Selective A1-Adenosine Antagonist 1,3-Dipropyl-8-[2-(5,6-epoxy)norbornyl]- xanthine. Pfister, Juerg R.; Belardinelli, Luiz; Lee, Gavin; Lum, Robert T.; Milner, Peter; Stanley, William C.; Linden, Joel; Baker, Stephen P.; Schreiner, George (CV Therapeutics, Palo Alto, CA, 94304, USA). Journal of Medicinal Chemistry, 40(12), 1773-1778 (English) 1997. CODEN: JMCMAR. ISSN: 0022-2623. Publisher: American Chemical Society.

AB The individual enantiomers I and II of the potent and highly selective racemic A1-adenosine antagonist 1,3-dipropyl-8-[2-(5,6-epoxy)norbornyl]xanthine (ENX) were synthesized utilizing asym. Diels-Alder cycloaddns. for the construction of the norbornane moieties. The binding affinities of the enantiomers and the racemate at guinea pig, rat, and cloned human A1- and A2a-adenosine receptor subtypes were detd. The S-enantiomer appears to be one of the more potent and clearly the most A1-selective antagonist reported to date, with Ki values of 0.67 and 0.45 nM, resp., at the rat and cloned human A1-receptors and with 1800-fold (rat) and 2400-fold (human) subtype selectivity. Both enantiomers, administered i.v. to saline-loaded rats, induced diuresis via antagonism of renal A1-adenosine receptors.

IT 190316-06-4P

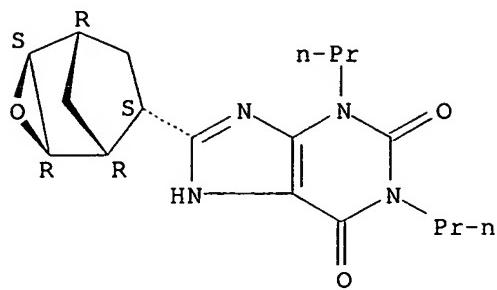
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)

(prepn. of dipropyl[(epoxy)norbornyl]xanthine enantiomers as A1-adenosine antagonists)

RN 190316-06-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl)-1,3-dipropyl-, [1R-(1.alpha.,2.beta.,4.beta.,5.alpha.,6.beta.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



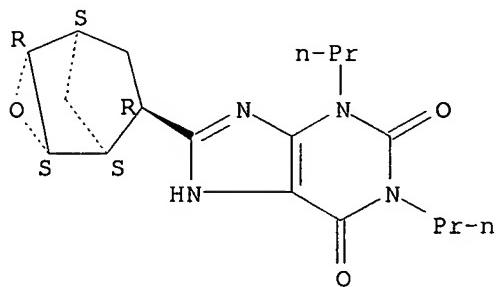
IT 166374-48-7P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(prep. of dipropyl[(epoxy)norbornyl]xanthine enantiomers as A1-adenosine antagonists)

RN 166374-48-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-oxatricyclo[3.2.1.02,4]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

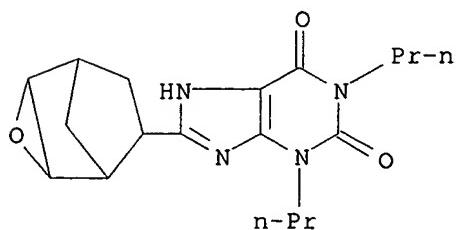


IT 166181-76-6

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(prep. of dipropyl[(epoxy)norbornyl]xanthine enantiomers as A1-adenosine antagonists)

RN 166181-76-6 HCPLUS

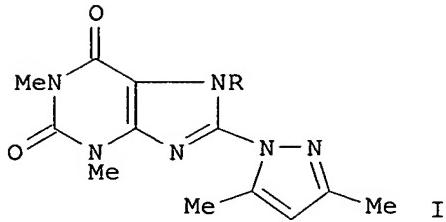
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.02,4]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



L5 ANSWER 50 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1997:297890 Document No. 126:330513 Synthesis and antiphlogistic effect of some 7-substituted 8-(3,5-dimethyl-1-pyrazolyl) theophyllines. Mazur, I. A.; Kremzer, O. A.; Korobko, D. B.; Samura, B. A.; Beljenkij, C. A. (Kiev. Derzhavn. Med. Univ., Kiev, Ukraine). Farmatsevtichni Zhurnal (Kiev) (3), 82-84 (Ukrainian) 1996. CODEN: FRZKAP. ISSN: 0367-3057. OTHER SOURCES: CASREACT 126:330513. Publisher: Zdorov'ya.

GI



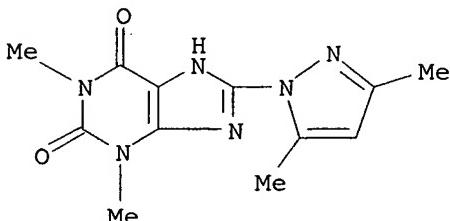
AB Fifteen title compds. I ( $R = H$ , alkyl, hydroxyalkyl, aryl), which showed effective antiinflammatory activity, were synthesized in 53.0-94.0% yield by cyclocondensation reaction of the corresponding 7-substituted 8-hydrazinotheophyllines with  $(MeCO)_2CH_2$  in refluxing glacial AcOH.

IT 145351-66-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and antiinflammatory activity of some substituted (dimethylpyrazolyl)theophyllines by cyclocondensation of hydrazinotheophyllines with acetylacetone)

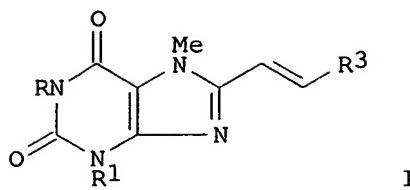
RN 145351-66-2 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(3,5-dimethyl-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 51 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1996:137307 Document No. 124:289082 (E)-1-(Heterocyclyl or cyclohexyl)-2-[1,3,7-trisubstituted (xanthin-8-yl)]ethenes as A2a adenosine receptor antagonists. Del Giudice, M. R.; Borioni, A.; Mustazza, C.; Gatta, F.; Dionisotti, S.; Zocchi, C.; Ongini, E. (Lab. Chim. Farm., Inst. Super Sanita, Rome, 00161, Italy). European Journal of Medicinal Chemistry, 31(1), 59-63 (English) 1996. CODEN: EJMCA5. ISSN: 0223-5234. Publisher: Elsevier.



**AB** Some 1,3,7-trisubstituted-8-styrylxanthine analogs I (R, R1 = Me, n-Pr; R3 = 3-furyl, 3-thienyl, 2-furyl, 2-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl), with the aryl group replaced by a heterocycle or cyclohexane ring, were prep'd. and evaluated for their interaction with the A1 and A2a adenosine receptors. The highest degree of activity was displayed by 1,3-dipropyl-7-methyl-8-[2-(3-thienyl)ethenyl]xanthine I (R = R1 = n-Pr, R3 = 3-thienyl), which was found to be a potent and selective A2a antagonist in binding assays ( $K_i = 19$  nM, A1/A2a ratio = 30).

**IT** 175727-36-3P 175727-37-4P 175727-38-5P  
 175727-39-6P 175727-40-9P 175727-41-0P  
 175727-42-1P 175727-43-2P 175727-44-3P  
 175727-45-4P 175727-46-5P 175727-47-6P  
 175727-49-8P 175727-50-1P

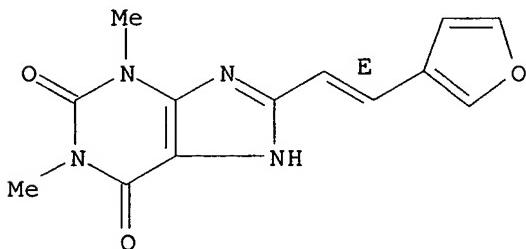
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prep'n. and adenosine receptor A2a antagonist activity of heterocyclyl-substituted xanthinylethenes)

**RN** 175727-36-3 HCAPLUS

**CN** 1H-Purine-2,6-dione, 8-[2-(3-furanyl)ethenyl]-3,7-dihydro-1,3-dimethyl-, (E)- (9CI) (CA INDEX NAME)

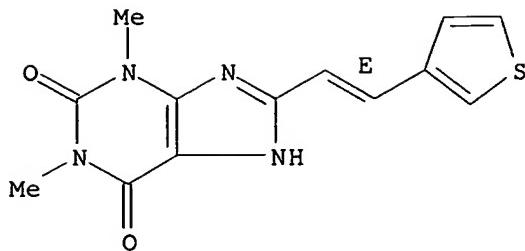
Double bond geometry as shown.



**RN** 175727-37-4 HCAPLUS

**CN** 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[2-(3-thienyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

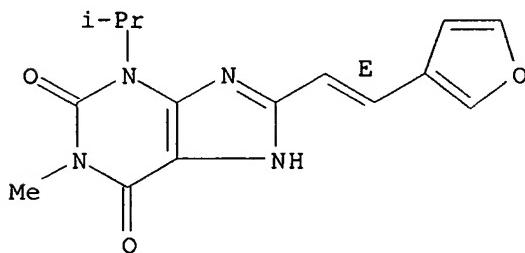
Double bond geometry as shown.



RN 175727-38-5 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(3-furanyl)ethenyl]-3,7-dihydro-1-methyl-3-(1-methylethyl)-, (E)- (9CI) (CA INDEX NAME)

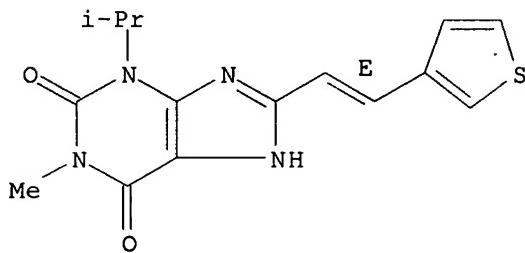
Double bond geometry as shown.



RN 175727-39-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-(1-methylethyl)-8-[2-(3-thienyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

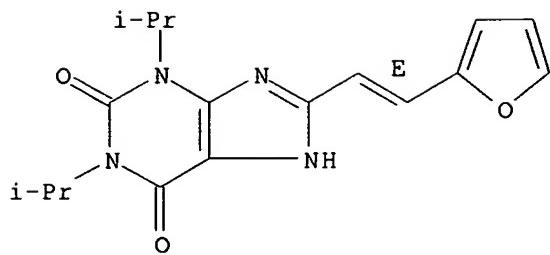
Double bond geometry as shown.



RN 175727-40-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(2-furanyl)ethenyl]-3,7-dihydro-1,3-bis(1-methylethyl)-, (E)- (9CI) (CA INDEX NAME)

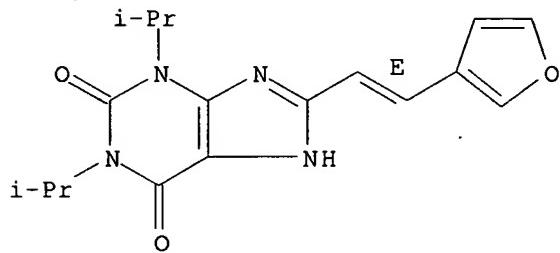
Double bond geometry as shown.



RN 175727-41-0 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(3-furanyl)ethenyl]-3,7-dihydro-1,3-bis(1-methylethyl)-, (E)- (9CI) (CA INDEX NAME)

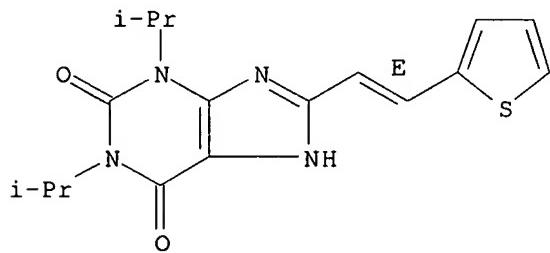
Double bond geometry as shown.



RN 175727-42-1 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-bis(1-methylethyl)-8-[2-(2-thienyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

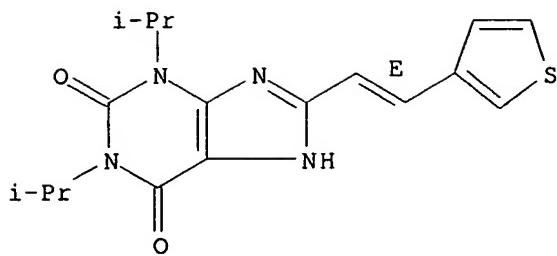
Double bond geometry as shown.



RN 175727-43-2 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-bis(1-methylethyl)-8-[2-(3-thienyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

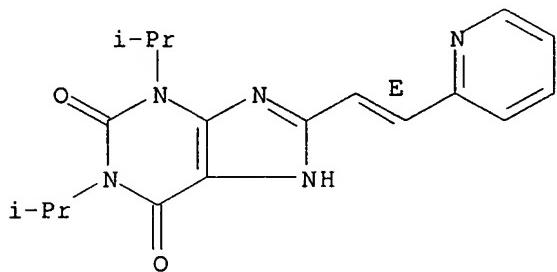
Double bond geometry as shown.



RN 175727-44-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-bis(1-methylethyl)-8-[2-(2-pyridinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

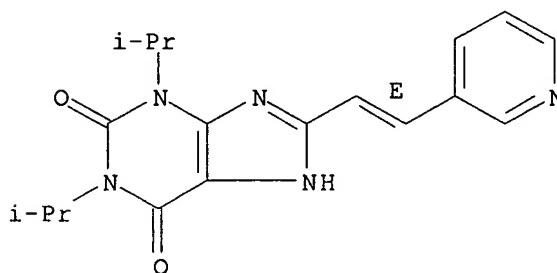
Double bond geometry as shown.



RN 175727-45-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-bis(1-methylethyl)-8-[2-(3-pyridinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

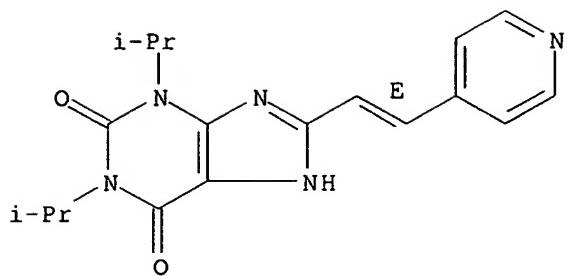
Double bond geometry as shown.



RN 175727-46-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-bis(1-methylethyl)-8-[2-(4-pyridinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

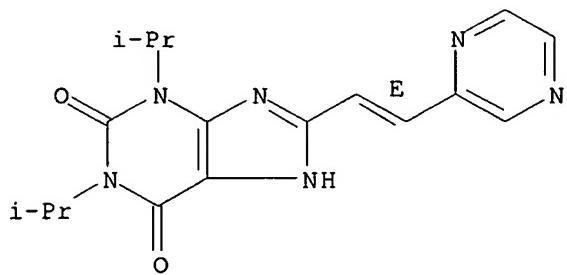
Double bond geometry as shown.



RN 175727-47-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-bis(1-methylethyl)-8-(2-pyrazinylethenyl)-, (E)- (9CI) (CA INDEX NAME)

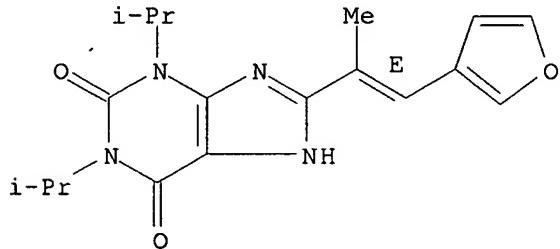
Double bond geometry as shown.



RN 175727-49-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(3-furanyl)-1-methylethenyl]-3,7-dihydro-1,3-bis(1-methylethyl)-, (E)- (9CI) (CA INDEX NAME)

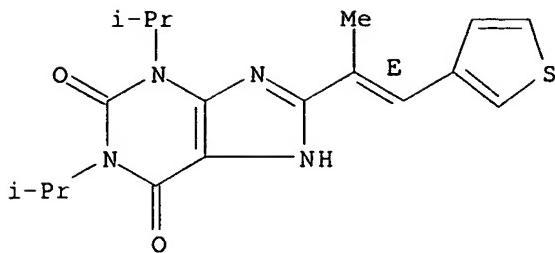
Double bond geometry as shown.



RN 175727-50-1 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-bis(1-methylethyl)-8-[1-methyl-2-(3-thienyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

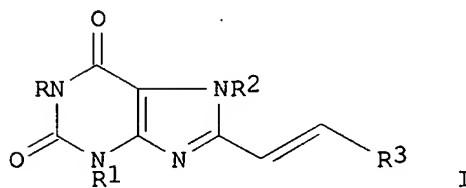
Double bond geometry as shown.



L5 ANSWER 52 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1996:113590 Document No. 124:289111 Preparation of xanthine derivatives for treatment of Parkinson's disease. Suzuki, Fumio; Shimada, Junichi; Koike, Nobuaki; Nakamura, Joji; Shioazaki, Shizuo; Ichikawa, Shunji; Ishii, Akio; Nonaka, Hiromi (Kyowa Hakko Kogyo Co., Ltd., Japan). U.S. US 5484920 A 19960116, 61 pp. Cont.-in-part of U.S. Ser. No. 42,535, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1993-133510 19931007. PRIORITY: JP 1992-257834 19920928; US 1993-42535 19930405; JP 1993-236176 19930922.

GI



AB Xanthines I [R, R1 = Me, Et; R2 = H, alkyl; R3 = substituted Ph] were prep'd. as selective adenosine A2 antagonists. Thus, 5,6-diamino-1,3-diethyluracil was treated with 3,4-dimethoxycinnamic acid to give I [R = R1 = Et, R2 = H, R3 = 3,4-(MeO)2C6H3] which at 1X10-5 M caused 98% inhibition of A2 receptor activity.

IT 151539-58-1P 151539-61-6P 155271-12-8P

155271-18-4P 155814-31-6P

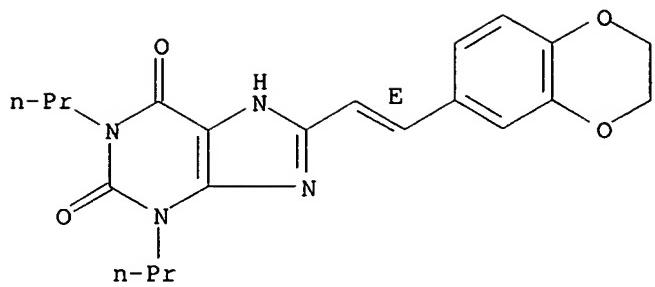
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of arylvinylxanthines as selective A2 receptor antagonists)

RN 151539-58-1 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethenyl]-3,7-dihydro-1,3-dipropyl-, (E)- (9CI) (CA INDEX NAME)

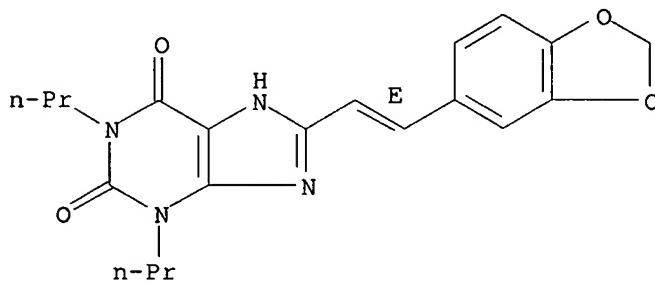
Double bond geometry as shown.



RN 151539-61-6 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-3,7-dihydro-1,3-dipropyl-, (E)- (9CI) (CA INDEX NAME)

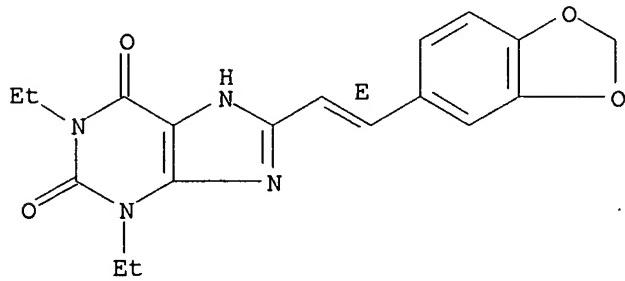
Double bond geometry as shown.



RN 155271-12-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-1,3-diethyl-3,7-dihydro-, (E)- (9CI) (CA INDEX NAME)

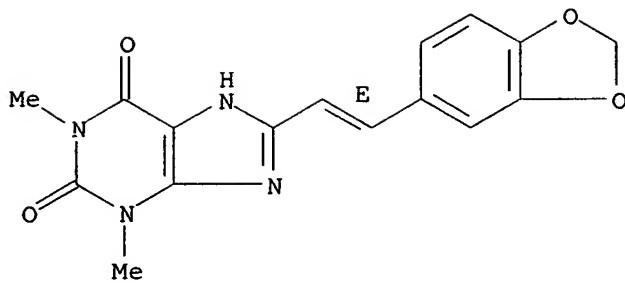
Double bond geometry as shown.



RN 155271-18-4 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-3,7-dihydro-1,3-dimethyl-, (E)- (9CI) (CA INDEX NAME)

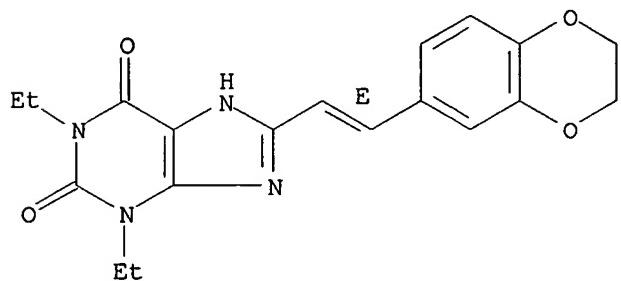
Double bond geometry as shown.



RN 155814-31-6 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethenyl]-1,3-diethyl-3,7-dihydro-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 155271-88-8P 155271-99-1P

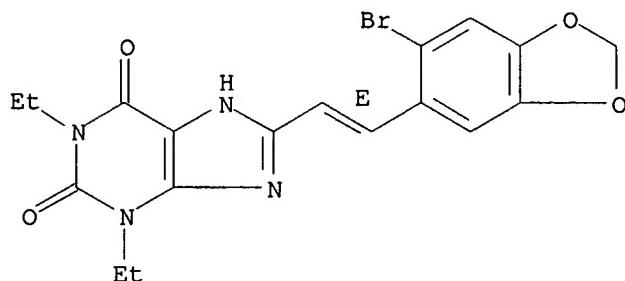
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
USES (Uses)

(prep. of arylvinylxanthines as selective A2 receptor antagonists)

RN 155271-88-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(6-bromo-1,3-benzodioxol-5-yl)ethenyl]-1,3-diethyl-3,7-dihydro-, (E)- (9CI) (CA INDEX NAME)

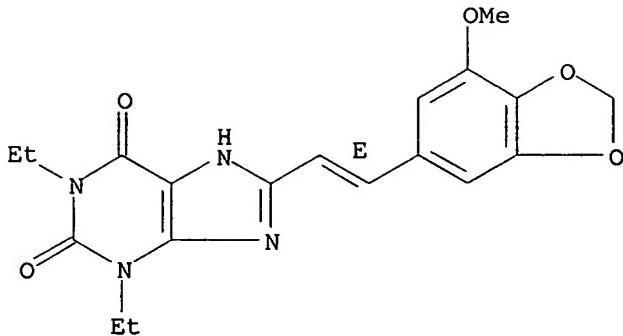
Double bond geometry as shown.



RN 155271-99-1 HCPLUS

CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[2-(7-methoxy-1,3-benzodioxol-5-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L5 ANSWER 53 OF 163 HCPLUS COPYRIGHT 2002 ACS

1996:18861 Document No. 124:135440 1,3-Dipropyl-8-[2-(5,6-epoxy)norbornyl]xanthine, a potent, specific and selective A1 adenosine receptor antagonist in the guinea pig heart and brain and in DDT1MF-2 cells. Belardinelli, Luiz; Shryock, John C.; Zhang, Yi; Schammells, Peter J.; Olsson, Ray; Dennis, Donn; Milner, Peter; Pfister, Juerg; Baker, Stephen P. (College of Medicine, University of Florida, Gainesville, FL, USA). Journal of Pharmacology and Experimental Therapeutics, 275(3), 1167-76 (English) 1995. CODEN: JPETAB. ISSN: 0022-3565. Publisher: Williams & Wilkins.

AB The objective of this study was to characterize the adenosine receptor (AdoR) antagonistic properties of a newly synthesized alkylxanthine, 1,3-dipropyl-8-[2-(5,6-epoxy)norbornyl]xanthine (ENX), and compare them to those of 1,3-dipropyl-8-(cyclopentyl)xanthine (CPX), 1,3-dipropyl-8-(3-noradamantyl)xanthine (NAX) and (.-.)-N6-endo-norbornan-2-yl-9-methyladenine (N-0861). The potencies and selectivities of ENX, CPX, NAX and N-0861 were detd. by functional studies of guinea pig isolated perfused hearts, and by radioligand binding assays for A1 and A2a AdoRs in the guinea pig forebrain and striatum. ENX competitively antagonized A1 AdoR-mediated prolongations of atrioventricular nodal conduction time caused by Ado or by 2-chloro-N6-cyclopentyladenosine, but not those caused by carbachol (0.14 .mu.M) or MgCl<sub>2</sub> (3 mM). Schild anal. of 2-chloro-N6-cyclopentyladenosine-antagonist competition curves yielded pA<sub>2</sub> values for ENX, CPX and NAX of 8.45, 8.55 and 8.79, resp. ENX (30 .mu.M) and N-0861 (30 .mu.M) did not attenuate the A2 AdoR-mediated increase in coronary conductance caused by adenosine. CPX and NAX attenuated the coronary vasodilation caused by adenosine with IC<sub>50</sub> values of 1.5 and 7.1 .mu.M, resp. Radioligand binding assays revealed that ENX, CPX and NAX and N-0861 had a 400-, 209-, 110- and 10-fold greater affinity, resp., for A1 than for A2a AdoRs of guinea pig brain membranes. Thus, ENX was equipotent with CPX and NAX and more potent than N-0861 (pA<sub>2</sub> = 6.2) as an antagonist at A1 AdoRs, but had lower affinity for A2 AdoRs in guinea pig hearts and brain striatum than did either CPX or NAX. In DDT1 MF-2 cells, all three alkylxanthines had similar affinities for A1 AdoRs, whereas the affinity of N-0861 for A1 AdoRs was significantly lower. ENX appears to be the most A1 AdoR subtype-selective of the alkylxanthine class of AdoR antagonists reported to date.

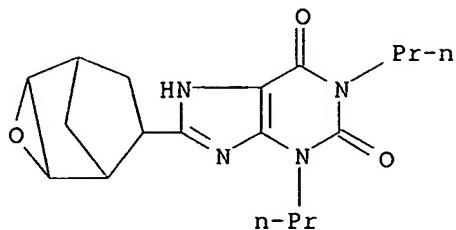
IT 166181-76-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(epoxy norbornyl xanthine deriv. as a potent, specific and selective A1 adenosine receptor antagonist in guinea pig heart and brain and in DDT1MF-2 cells)

RN 166181-76-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



L5 ANSWER 54 OF 163 HCPLUS COPYRIGHT 2002 ACS

1995:877911 Document No. 124:222 Structure-activity relationships in a series of 8-substituted xanthines as bronchodilator and A1-adenosine receptor antagonists. Corsano, Stefano; Strappaghetti, Giovannella; Scapicchi, Rossana; Lucacchini, Antonio; Senatore, Generoso (Istituto Chimica Farmaceutica Tecnica Farmaceutica, Universita Perugia, Perugia, 06123, Italy). Archiv der Pharmazie (Weinheim, Germany), 328(9), 654-8 (English) 1995. CODEN: ARPMAS. ISSN: 0365-6233. OTHER SOURCES: CASREACT 124:222. Publisher: VCH.

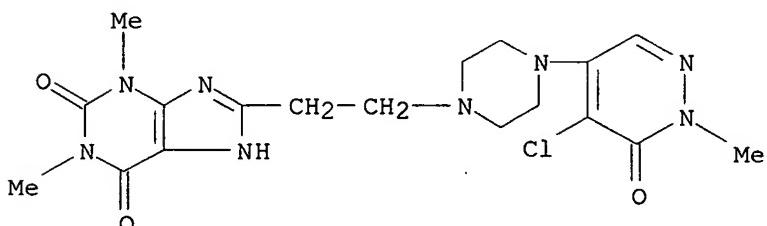
AB Four new derivs. of 8-piperazine Et xanthine were synthesized and their bronchospasmolytic activity and A1-adenosine affinity were studied. Their relaxant action in the tracheal muscle was lower than that of theophylline and that of theophylline derivs. substituted at the 7-position. Only one compd. where the Me group in the 1-position of the theophylline was substituted by an iso-Bu group showed a good affinity towards the A1-adenosine receptor.

IT 171115-07-4P 171115-08-5P 171115-10-9P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(structure-activity relationships of a series of 8-substituted xanthines as bronchodilator and A1-adenosine receptor antagonists)

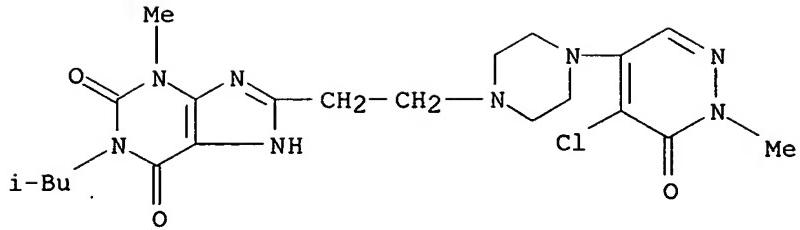
RN 171115-07-4 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(5-chloro-1,6-dihydro-1-methyl-6-oxo-4-pyridazinyl)-1-piperazinyl]ethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



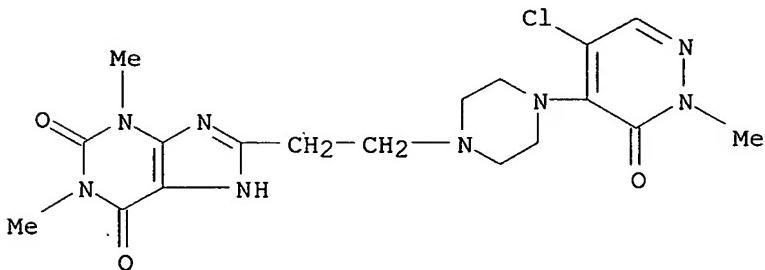
RN 171115-08-5 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(5-chloro-1,6-dihydro-1-methyl-6-oxo-4-pyridazinyl)-1-piperazinyl]ethyl]-3,7-dihydro-3-methyl-1-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 171115-10-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(5-chloro-2,3-dihydro-2-methyl-3-oxo-4-pyridazinyl)-1-piperazinyl]ethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

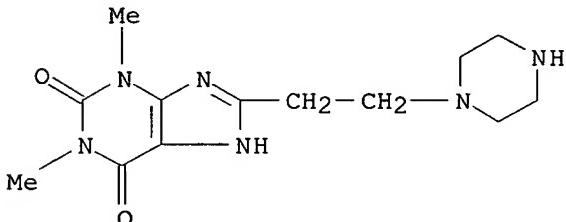


IT 171115-09-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (structure-activity relationships of a series of 8-substituted xanthines as bronchodilator and A<sub>1</sub>-adenosine receptor antagonists)

RN 171115-09-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[2-(1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

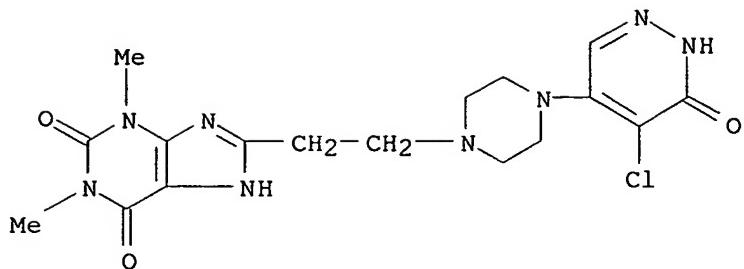


IT 171115-06-3P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
 (structure-activity relationships of a series of 8-substituted xanthines as bronchodilators and A<sub>1</sub>-adenosine receptor antagonists)

RN 171115-06-3 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(5-chloro-1,6-dihydro-6-oxo-4-pyridazinyl)-1-piperazinyl]ethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 55 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1995:731731 Document No. 123:143545 Preparation of novel A1 adenosine receptor agonists and antagonists. Belardinelli, Luiz; Olsson, Ray; Baker, Stephen; Scammells, Peter J.; Milner, Peter Gerard; Pfister, Jurg Roland; Schreiner, George Frederic (University of Florida, USA). PCT Int. Appl. WO 9511904 A1 19950504, 46 pp. DESIGNATED STATES: W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2.

APPLICATION: WO 1994-US12388 19941028. PRIORITY: US 1993-144459 19931028.

GI For diagram(s), see printed CA Issue.

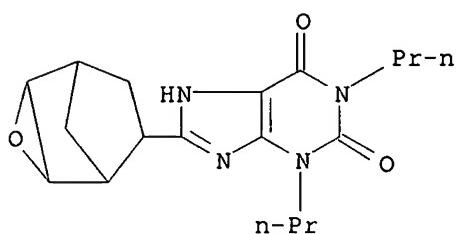
AB Prepn. of adenosine and xanthine derivs. I (R1, R2 = C1-C4 alkyl, n = 0-4, H, etc.) and II (R1, R2 = H, C1-C4 alkyl, R3 = O, C1-C4 alkyl, n = 0-4, etc.) and compns. comprising those compds. as potent selective agonists and antagonists of adenosine receptors are presented. The derivs. and compns. are used to treat conditions, including certain cardiac arrhythmias.

IT 166181-76-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. and adenosine receptor agonist and antagonist activity of xanthines)

RN 166181-76-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



IT 166374-48-7 166374-49-8

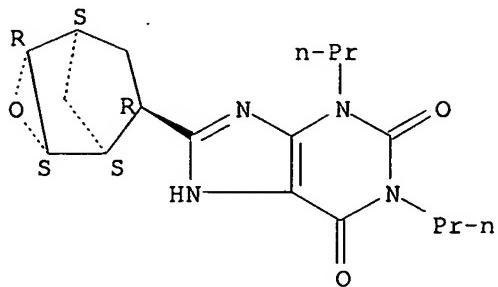
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prepn. and adenosine receptor agonist and antagonist activity of xanthines)

RN 166374-48-7 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6R)-3-

oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

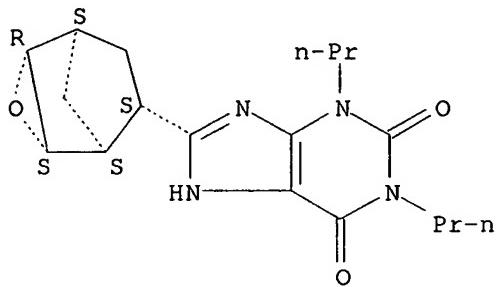
Absolute stereochemistry. Rotation (+).



RN 166374-49-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1S,2R,4S,5S,6S)-3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl-1,3-dipropyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

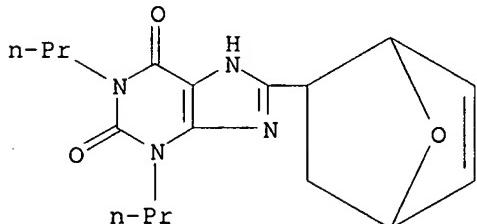


IT 166181-78-8P 166181-79-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. and adenosine receptor agonist and antagonist activity of xanthines)

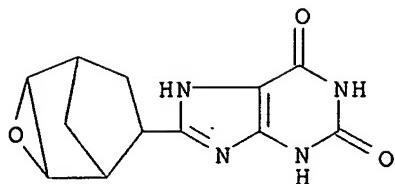
RN 166181-78-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(7-oxabicyclo[2.2.1]hept-5-en-2-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 166181-79-9 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-oxatricyclo[3.2.1.0<sub>2,4</sub>]oct-6-yl)-, (1.alpha.,2.beta.,4.beta.,5.alpha.,6.beta.)- (9CI) (CA INDEX NAME)



L5 ANSWER 56 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1995:560813 Document No. 123:111738 Synthesis and in vitro bronchospasmolytic activity of 8-aryl, heteroaryl or arylalkyl theophyllines. Baziard-Mouyset, G.; Rached, A.; Younes, S.; Tournaire, C.; Stigliani, J. L.; Payard, M.; Yavo, J. C.; Advenier, C. (Dep. Chim. Pharm., Fac. Pharm., Toulouse, 31400, Fr.). European Journal of Medicinal Chemistry, 30(3), 253-60 (English) 1995. CODEN: EJMCA5. ISSN: 0223-5234. Publisher: Elsevier.

AB Twenty-four 8-aryltheophyllines or 8-heteroaryl theophyllines were prep'd. The substituents are arom. rings and heterocycles likely to induce an antiallergic effect or a bronchospasmolytic activity. In vitro evaluation of the bronchospasm caused by acetylcholine or histamine shows an interesting activity for half of the compds. Among them, the 8-(2-furyl)- and 8-(2-chlorophenyl)theophylline derivs. are, for instance, four times more active than theophylline.

IT 20886-69-5P 33797-74-9P, 1H-Purine-2,6-dione,  
8-(2-furanyl)-3,7-dihydro-1,3-dimethyl 166115-55-5P

166115-57-7P 166115-58-8P 166115-60-2P

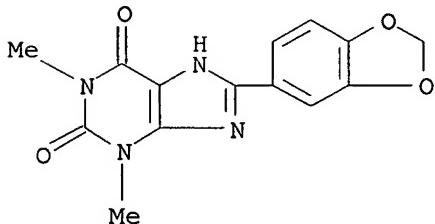
166115-61-3P 166115-62-4P 166115-63-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of theophylline derivs. as antiallergics or bronchospasmolytics)

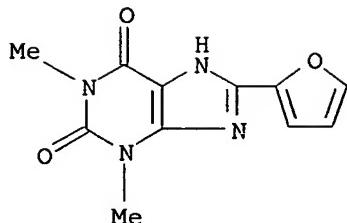
RN 20886-69-5 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(1,3-benzodioxol-5-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



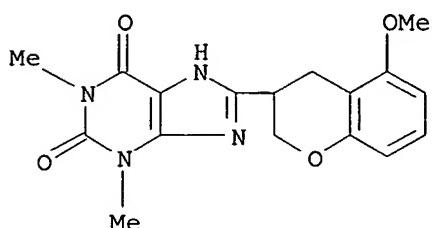
RN 33797-74-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



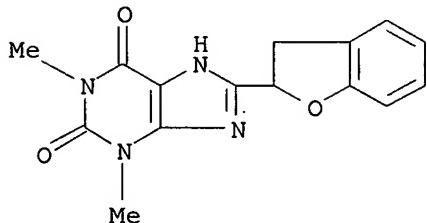
RN 166115-55-5 HCPLUS

CN 1H-Purine-2,6-dione, 8-(3,4-dihydro-5-methoxy-2H-1-benzopyran-3-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



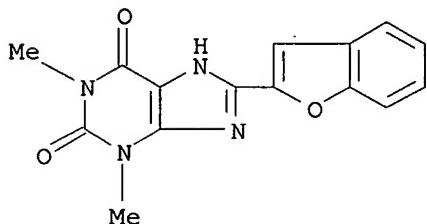
RN 166115-57-7 HCPLUS

CN 1H-Purine-2,6-dione, 8-(2,3-dihydro-2-benzofuranyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



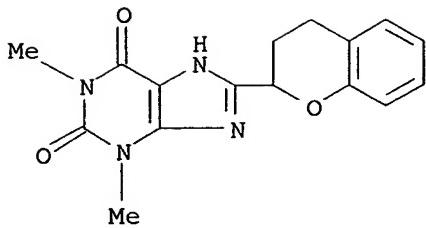
RN 166115-58-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-(2-benzofuranyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



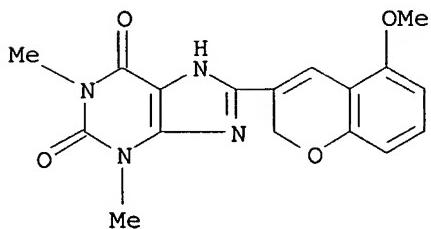
RN 166115-60-2 HCPLUS

CN 1H-Purine-2,6-dione, 8-(3,4-dihydro-2H-1-benzopyran-2-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



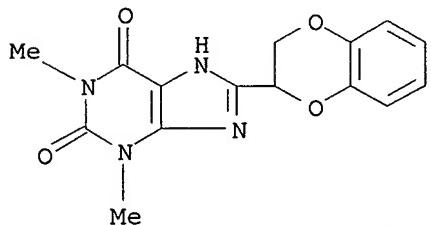
RN 166115-61-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(5-methoxy-2H-1-benzopyran-3-yl)-1,3-dimethyl- (9CI) (CA INDEX NAME)



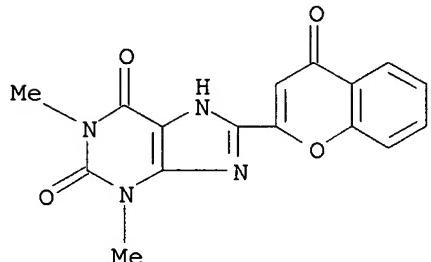
RN 166115-62-4 HCPLUS

CN 1H-Purine-2,6-dione, 8-(2,3-dihydro-1,4-benzodioxin-2-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 166115-63-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-oxo-4H-1-benzopyran-2-yl)- (9CI) (CA INDEX NAME)



L5 ANSWER 57 OF 163 HCPLUS COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 1E01

1995:509887 Document No. 122:281454 De Novo analysis of receptor binding affinity data of xanthine adenosine receptor antagonists. Dalpiaz, A.; Gardenghi, A.; Borea, P. A. (Ist. Farmacologia, Univ. Ferrara, Ferrara, Italy). Arzneimittel-Forschung, 45(3), 230-3 (English) 1995. CODEN: ARZNAD. ISSN: 0004-4172. Publisher: Cantor.

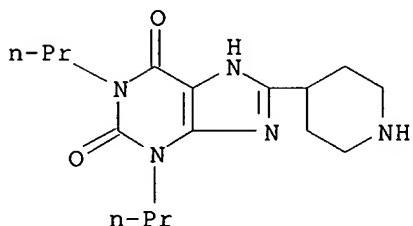
AB The receptor binding affinity data to adenosine A1 and A2 receptors of a wide series of xanthine derivs. have been analyzed for QSAR by the Free-Wilson model. The anal. of the individual group contribution shows, for both A1 and A2 receptors, the primary importance of the presence of bulky substituents at position 8 for an optimum receptor binding. Moreover, considering the different  $a_{ij}$  contributions of bulky substituents at position 8 for affinity to A1 with respect to A2 receptors, this position appears to be the most important for the synthesis of highly A1 selective xanthine derivs. Moreover the anal. of group contributions for other substitution positions of the xanthine moiety allows to state that suitable substitutions at positions 3 and 7 could confer some degree of A2 selectivity.

IT 108653-59-4 112683-71-3

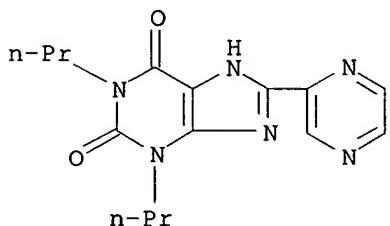
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(QSAR anal. of receptor binding affinity data of xanthine adenosine receptor antagonists)

RN 108653-59-4 HCPLUS

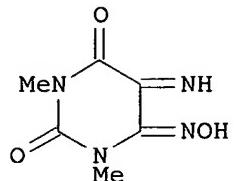
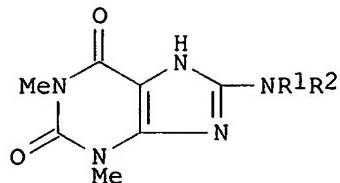
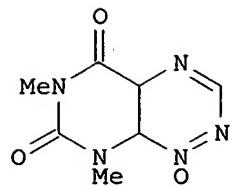
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-pyrazinyl- (9CI) (CA INDEX NAME)



1995:334057 Document No. 122:187223 Purines, pyrimidines and condensed systems based on them. 13. Conversion of ferenuline 1-oxide to 8-(dialkylamino)theophyllines by reaction with dialkylamines. Gulevskaya, A. V.; Pozharsky, A. F.; Shvidchenko, S. V. (Rostov. Gos. Univ., Rostov-on-Don, 344104, Russia). Khimiya Geterotsiklicheskikh Soedinenii (9), 1253-7 (Russian) 1994. CODEN: KGSSAQ. ISSN: 0132-6244. Publisher:



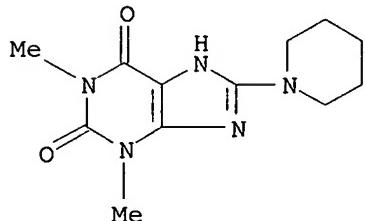
AB Fervenuline 1-oxide (I) reacted with secondary amines to give theophyllines (II; NR<sub>1</sub>R<sub>2</sub> = NMe<sub>2</sub>, NEt<sub>2</sub>, piperidino, morpholino). The reaction of I with NH<sub>3</sub> or MeNH<sub>2</sub> gave uracil deriv. III.

IT 961-48-8P 30958-49-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

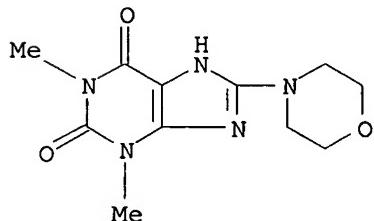
RN 961-48-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinyl)- (9CI)  
(CA INDEX NAME)



RN 30958-49-7 HCPLUS

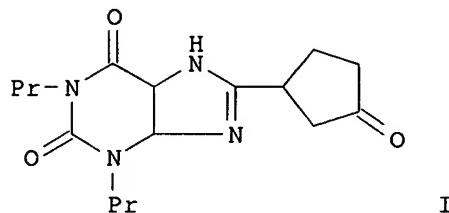
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- (9CI)  
(CA INDEX NAME)



L5 ANSWER 59 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1995:309013 Document No. 122:81397 Improved method for the preparation of 1,3-dipropyl-8-(3-oxocyclopentyl)xanthine. Kuefner-Muehl, Ulrike; Luettke, Sven (Boehringer Ingelheim KG, Germany). Ger. Offen. DE 4316576 A1 19941124, 4 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1993-4316576 19930518.

GI



I

AB The title compd., I (R enantiomer; m.p.170.5-1), useful as a pharmaceutical (no data), is prep'd. in high yield and with reduced need for chromatog. purifn. by the reaction of 2-carboxy-8,8-dimethyl-6,10-dioxaspiro[4.5]decane with 1,3-dipropyl-4,5-diaminouracil, the obtained amide intermediate is cyclized in aq. LiOH, and the protecting group is cleaved under acidic conditions.

IT 160430-53-5P 160430-56-8P

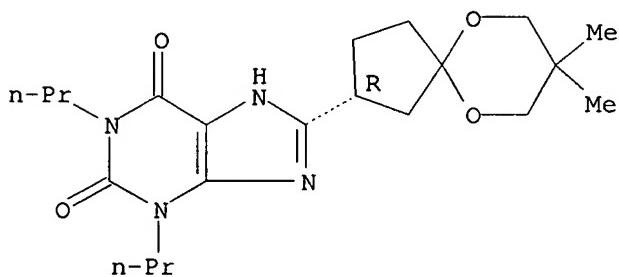
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(improved method for the prepn. of 1,3-dipropyl-8-(3-oxocyclopentyl)xanthine)

RN 160430-53-5 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(8,8-dimethyl-6,10-dioxaspiro[4.5]dec-2-yl)-3,7-dihydro-1,3-dipropyl-, (R)- (9CI) (CA INDEX NAME)

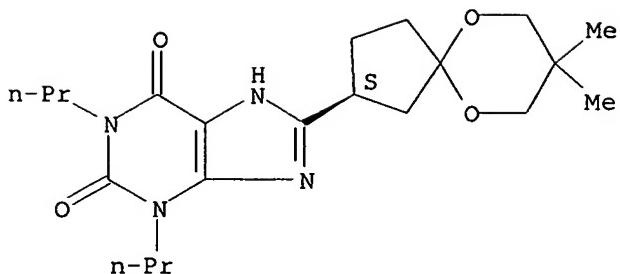
Absolute stereochemistry.



RN 160430-56-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(8,8-dimethyl-6,10-dioxaspiro[4.5]dec-2-yl)-3,7-dihydro-1,3-dipropyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 60 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1995:262387 Document No. 122:52648 A quantitative analysis of binding affinities of ligands active at adenosine receptors. Sharma, R. C.; Singh, P.; Ojha, T. N.; Tiwari, S. (Dep. Chem., S.K. Government College, Sikar, 332 001, India). Drug Design and Discovery, 12(2), 169-77 (English) 1994. CODEN: DDDIEV. ISSN: 1055-9612. Publisher: Harwood.

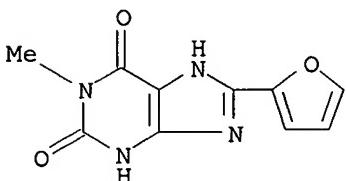
AB Binding affinities, pKi's, of 1,3-dipropyl-8-phenylxanthines and 8-substituted xanthines as selective antagonists at A1- A2- adenosine receptors, were quant. analyzed in terms of hydrophobic parameter, .pi., and van der Waals vol. (Vw). For ligands of the first series, the hydrophobicity of para-substituents and the bulk of meta-substituents are shown to be the deciding factors. Similarly, for the other series, the binary substitutions at X-, Y- and R-positions, highlighted by resp. dummy variables, and the bulk rendered by groups at R1-position, are significantly correlated with A1- and A2-receptor affinities. Addnl., the Free-Wilson study of this series resulting into individual substituent contribution, provides similar interferences to these, but in a more exact manner. This study also hints at the possibility of a different accommodation site at the receptor for the R1-substituents of the congeners on account of conformational dissimilarity of A1- and A2-receptors.

IT 160070-46-2 160070-47-3 160070-50-8  
160070-51-9 160070-52-0 160070-53-1  
160070-54-2

RL: PRP (Properties)  
(quant. anal. of binding affinities of ligands active at adenosine receptors)

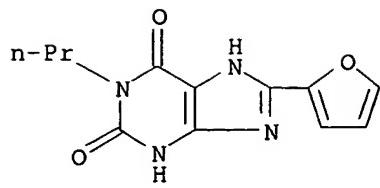
RN 160070-46-2 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



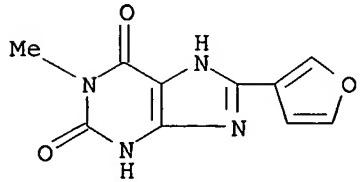
RN 160070-47-3 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1-propyl- (9CI) (CA INDEX NAME)



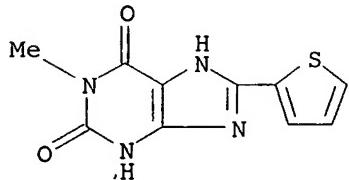
RN 160070-50-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(3-furanyl)-3,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



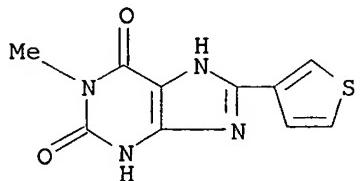
RN 160070-51-9 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



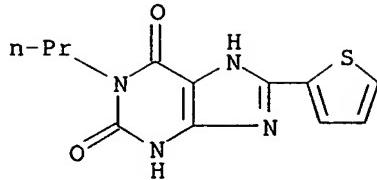
RN 160070-52-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)

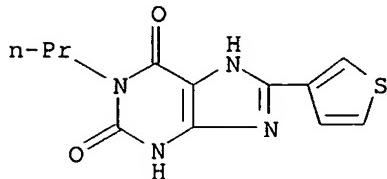


RN 160070-53-1 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-propyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)

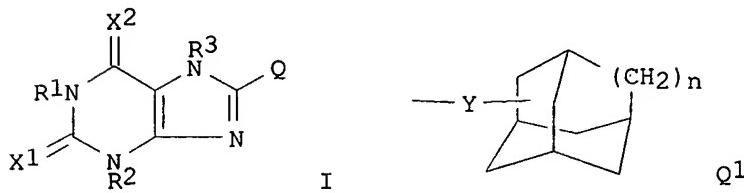


RN 160070-54-2 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1-propyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 61 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1994:700909 Document No. 121:300909 Xanthine derivatives. Suzuki, Fumio; Shimada, Junichi; Ishii, Akio; Ohno, Tetsuji; Karasawa, Akira; Kubo, Kazuhiro; Nonaka, Hiromi (Kyowa Hakko Kogyo Co., Ltd., Japan). U.S. US 5290782 A 19940301, 22 pp. Cont.-in-part of U.S. Ser No. 574,447, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1992-839690 19920224. PRIORITY: JP 1989-226642 19890901; US 1990-574447 19900829; JP 1991-29796 19910225.

GI



AB Novel xanthine compds. I [X<sub>1</sub>, X<sub>2</sub> independently = O, S; Q = Q1; Y = a single bond or alkylene; n = 0, 1; each of R<sub>1</sub> and R<sub>2</sub> independently = H, lower alkyl, allyl or propargyl, and R<sub>3</sub> represents hydrogen or lower alkyl, provided that when Q is adamantyl, then R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are not simultaneously Me] and pharmaceutically acceptable salts thereof are claimed. I have a diuretic effect, a renal-protecting effect and a bronchodilating effect. In a preparative example, treating 3-noradamantanecarboxylic acid 1.65 g with SOC<sub>12</sub> 0.08 mL in pyridine 20 mL and then with 5,6-diamino-1,3-diallyluracil 2.00 g gave 73% 6-amino-1,3-diallyl-5-(noradamante-3-carbonylamino)uracil, which was cyclized with aq. NaOH in dioxane to give 71% 1,3-diallyl-8-(3-noradamantyl)xanthine (II). Pharmaceutical formulations are given. In a

pharmacol. test, II increased urine prodn. 109% and Na<sup>+</sup> excretion 99% at 0.40 mg/kg dosage in male rats.

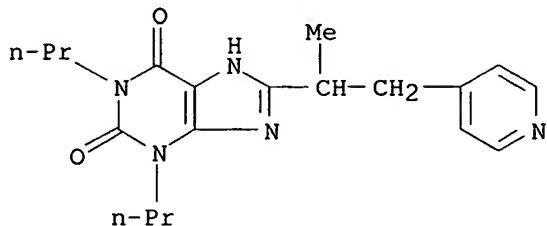
IT 136198-96-4P 136198-97-5P 136198-98-6P

136198-99-7P 136199-01-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as bronchodilating and renal-protecting drug)

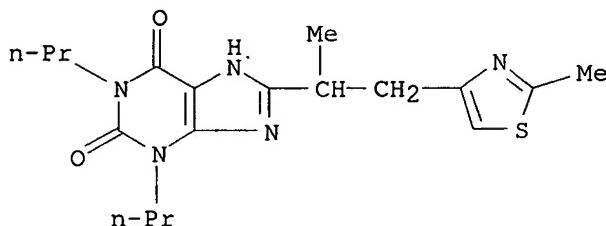
RN 136198-96-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[1-methyl-2-(4-pyridinyl)ethyl]-1,3-dipropyl- (9CI) (CA INDEX NAME)



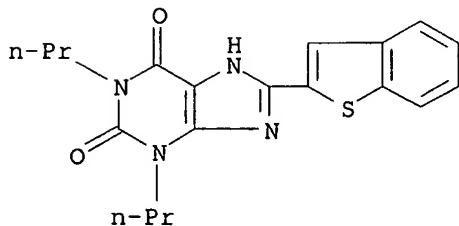
RN 136198-97-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[1-methyl-2-(2-methyl-4-thiazolyl)ethyl]-1,3-dipropyl- (9CI) (CA INDEX NAME)



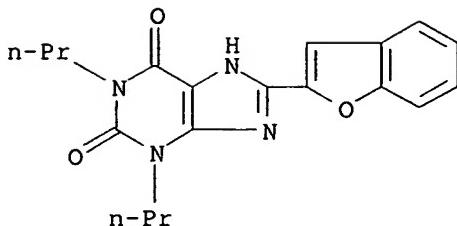
RN 136198-98-6 HCAPLUS

CN 1H-Purine-2,6-dione, 8-benzo[b]thien-2-yl-3,7-dihydro-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



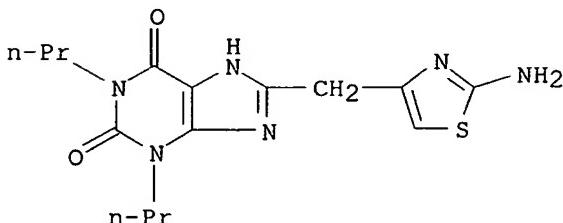
RN 136198-99-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-benzofuranyl)-3,7-dihydro-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



RN 136199-01-4 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(2-amino-4-thiazolyl)methyl]-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



L5 ANSWER 62 OF 163 HCAPLUS COPYRIGHT 2002 ACS

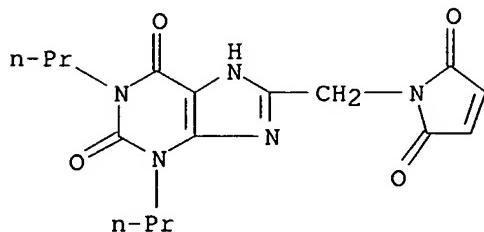
1994:524596 Document No. 121:124596 Substituted 1,3-Dipropylxanthines as Irreversible Antagonists of A1 Adenosine Receptors. Scammells, Peter J.; Baker, Stephen P.; Belardinelli, Luiz; Olsson, Ray A. (Department of Internal Medicine, University of South Florida, Tampa, FL, 33612, USA). Journal of Medicinal Chemistry, 37(17), 2704-12 (English) 1994. CODEN: JMCMAR. ISSN: 0022-2623.

AB This report describes the synthesis of 29 xanthines contg. a chemoreactive chloroaryl, .beta.-chloroethylamino, .alpha.,.beta.-unsatd. carbonyl, bromoacetyl, 3-(fluorosulfonyl)benzoyl, or 4-(fluorosulfonyl)benzoyl group as part of an exocyclic 1-, 3-, or 8-substituent. The xanthines inhibited the binding of [<sup>3</sup>H]-8-cyclopentyl-1,3-dipropylxanthine ([<sup>3</sup>H]CPX) to the A1 adenosine receptor (A1AR) of DDT1 MF2 cells at IC<sub>50</sub>s in the low-nanomolar to low-micromolar range. Seven of the 29 analogs irreversibly inhibited the binding of [<sup>3</sup>H]CPX without changing the KD of that ligand; five were 1,3-dipropylxanthines having the following reactive groups as 8-substituents: (bromoacetamido)methyl (24), (bromoacetamido)ethyl (25), (bromoacetamido)propyl (26), [4-(fluorosulfonyl)benzamido]methyl (33) or 3-[[4-(fluorosulfonyl)benzoyl]oxy]cyclopentyl (42). Both 8-cyclopentyl-3-[3-[[4-(fluorosulfonyl)benzoyl]oxy]propyl]-1-propylxanthine (53) and 8-cyclopentyl-1,3-bis[3-[[4-(fluorosulfonyl)benzoyl]oxy]propyl]xanthine (55) inhibited [<sup>3</sup>H]CPX binding irreversibly. Five of the ligands, including 26, 33 (IC<sub>50</sub> = 49 .mu.M), and 53 (IC<sub>50</sub> = 9 .mu.M), antagonized the binding of [<sup>3</sup>H]NECA to the A2aAR of PC12 cells, but unlike binding to the A1AR, binding to the A2aAR was completely reversible. The potency of 33 (IC<sub>50</sub> = 2 .mu.M, 72% loss of CPX binding at 1 .mu.M) and 53 (IC<sub>50</sub> = 0.01 .mu.M, 74% loss of CPX binding at 0.05 .mu.M) and their selectivity for the A1AR suggest that those two ligands may be useful in studies of the structure and function of that receptor. Structure-activity relations are noted.

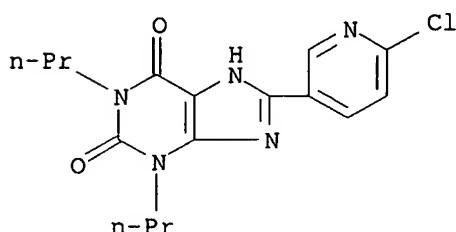
IT 156547-27-2P 156547-59-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. and adenosine-A1 receptor-antagonizing activity of, structure

in relation to)  
RN 156547-27-2 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)methyl]-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)

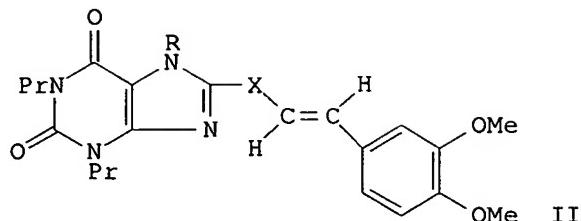
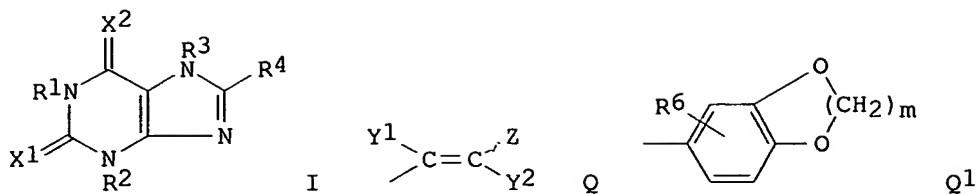


RN 156547-59-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-(6-chloro-3-pyridinyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



L5 ANSWER 63 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
1994:483358 Document No. 121:83358 preparation of xanthine derivatives as antidepressants. Suzuki, Fumio; Shimada, Junichi; Ishii, Akio; Nakamura, Joji; Ichikawa, Shunji; Kitamura, Shigeto; Koike, Nobuaki (Kyowa Hakko Kogyo Co., Ltd., Japan). PCT Int. Appl. WO 9401114 A1 19940120, 173 pp.  
DESIGNATED STATES: W: CA, JP, NO, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1993-JP931 19930707. PRIORITY: JP 1992-181025 19920708.

GI



**AB** Xanthine derivs. [I; R1, R2, R3 = H, alkyl, allyl, propargyl; R4 = cycloalkyl, -(CH<sub>2</sub>)nR5 (wherein R5 = optionally substituted aryl, heterocyclic group, and n = 0-4), Q (wherein Y1, Y2 = H, F, Me; Z = optionally substituted aryl, Q1 wherein R6 = H, OH, alkyl, alkoxy, halo, nitro or amino; m = 1-3), optionally substituted heterocyclic group; X1, X2 = O or S] are prep'd. A mixt. of 5,6-diamino-1,3-dipropyluracil, 3,4-dimethoxycinnamic acid, and 3-(3-diethylaminopropyl)-1-ethylcarbodiimide HCl in dioxane-H<sub>2</sub>O was stirred at room temp. and pH 5.5 to give 94% amide II (R = H, X = NHCO), which was refluxed with 1N NaOH in dioxane to give 77% styryl compd. II (R = H, X = bond) (III). Methylation of III with MeI and K<sub>2</sub>CO<sub>3</sub> in DMF at 50.degree. gave 98% Me deriv. II (R = Me, X = bond), which at 2.5 mg/kg p.o. in mice showed 4.8-fold increase in clonidine-induced aggression, vs. control.

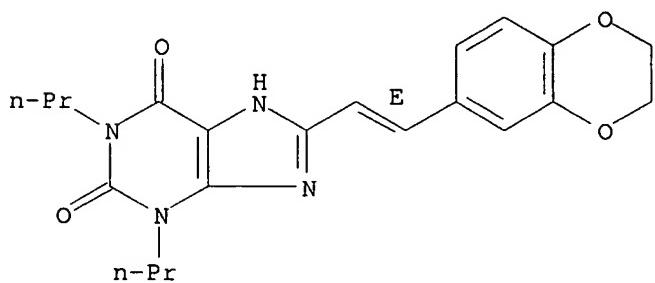
**IT** 151539-58-1P 151539-61-6P 155271-12-8P  
155271-18-4P 155271-88-8P 155271-99-1P  
155814-31-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, as antidepressant)

**RN** 151539-58-1 HCPLUS

**CN** 1H-Purine-2,6-dione, 8-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethenyl]-3,7-dihydro-1,3-dipropyl-, (E)- (9CI) (CA INDEX NAME)

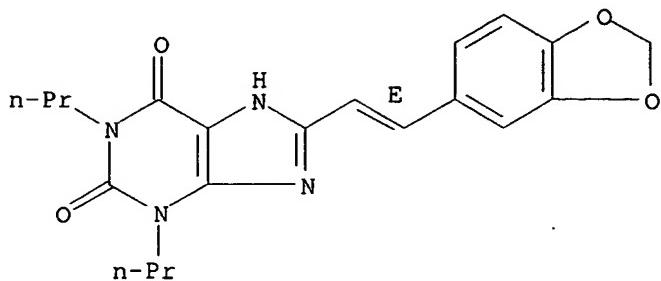
Double bond geometry as shown.



**RN** 151539-61-6 HCPLUS  
**CN** 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-3,7-dihydro-1,3-

dipropyl-, (E)- (9CI) (CA INDEX NAME)

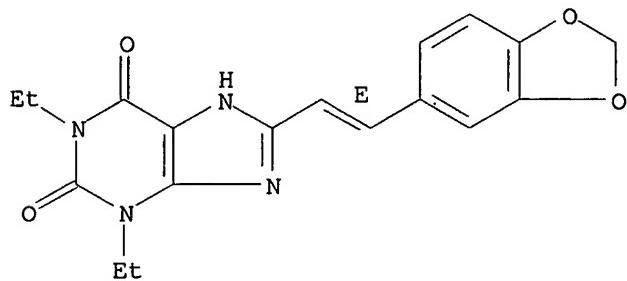
Double bond geometry as shown.



RN 155271-12-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-1,3-diethyl-3,7-dihydro-, (E)- (9CI) (CA INDEX NAME)

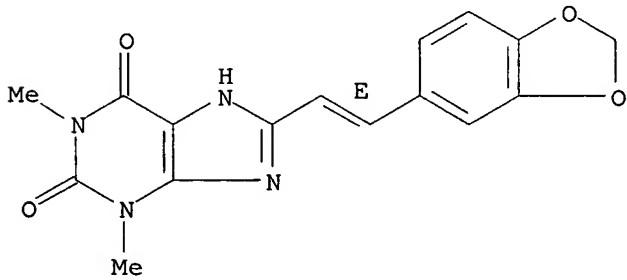
Double bond geometry as shown.



RN 155271-18-4 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-3,7-dihydro-1,3-dimethyl-, (E)- (9CI) (CA INDEX NAME)

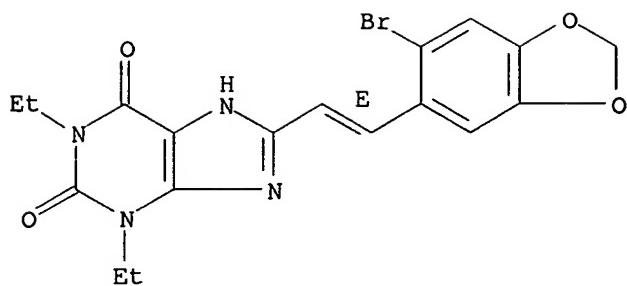
Double bond geometry as shown.



RN 155271-88-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(6-bromo-1,3-benzodioxol-5-yl)ethenyl]-1,3-diethyl-3,7-dihydro-, (E)- (9CI) (CA INDEX NAME)

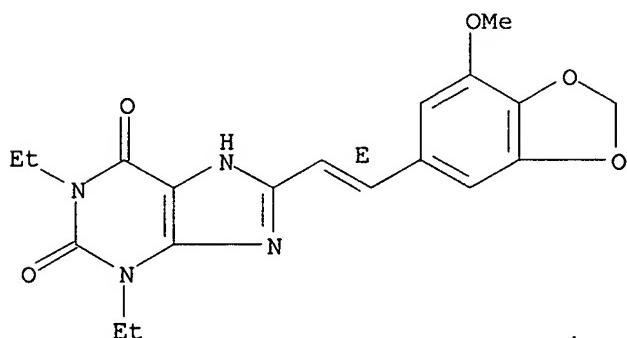
Double bond geometry as shown.



RN 155271-99-1 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[2-(7-methoxy-1,3-benzodioxol-5-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

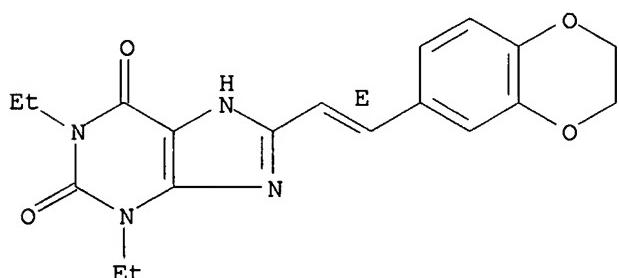
Double bond geometry as shown.



RN 155814-31-6 HCAPLUS

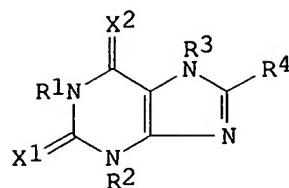
CN 1H-Purine-2,6-dione, 8-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethenyl]-1,3-diethyl-3,7-dihydro-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L5 ANSWER 64 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1994:400920 Document No. 121:920 Therapeutic agents for Parkinson's disease.  
 Suzuki, Fumio; Shimada, Junichi; Koike, Nobuaki; Nakamura, Joji; Shiozaki, Shizuo; Ichikawa, Shunji; Nonaka, Hiromi (Kyowa Hakko Kogyo Co., Ltd., Japan). Eur. Pat. Appl. EP 590919 A1 19940406, 82 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1993-307654 19930928. PRIORITY: JP 1992-257834 19920928.



**AB** Disclosed as therapeutic agents for Parkinson's disease are xanthine derivs. of the formula (I): in which: R1 and R2 each represent Me or ethyl; R3 represents hydrogen, C1-C6 straight or branched chain alkyl or C2-C6 straight or branched chain alkenyl or alkynyl; R4 represents C3-C6 cycloalkyl; a -(CH<sub>2</sub>)<sub>n</sub>-R5 group where n is 0 or an integer of from 1 to 4, and R5 represents Ph, naphthyl or a heterocyclic group or a substituted Ph, naphthyl or heterocyclic group contg. from 1-4 substituents selected from C1-C6 alkyl, C1-C6 alkoxy, hydroxy, halogen, nitro, amino, mono- or di-(C1-C6) alkylamino, trifluoromethyl, benzyloxy, Ph, phenoxy or C1-C6 alkoxy substituted by hydroxy, C1-C6 alkoxy, halogen, amino, azide, carboxy or (C1-C6 alkoxy) carbonyl; or a group were Y1 and Y2 each represent hydrogen, halogen, or C1-C6 straight or branched chain alkyl; and Z represents a group in which R6 represents hydrogen, hydroxy, C1-C6 straight or branched chain alkyl, C1-C6 straight or branched chain alkoxy, halogen, nitro, or amino, and m represents an integer of from 1 to 4, a Ph, naphthyl or heterocyclic group or a substituted Ph, naphthyl or heterocyclic group as defined under R5; and X1 and X2 each represent O or S; or a pharmaceutically acceptable salt thereof.

**IT** 155271-12-8P 155271-14-0P 155271-18-4P

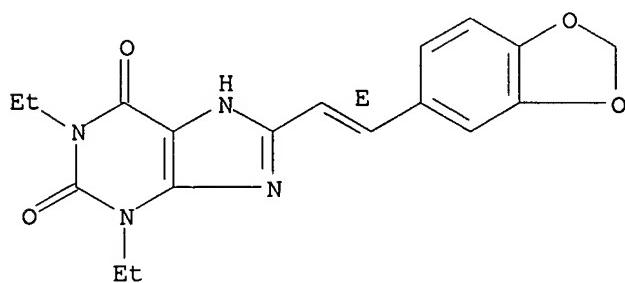
155271-88-8P 155271-99-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of, for treating Parkinson's disease)

RN 155271-12-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-1,3-dihydro-, (E)- (9CI) (CA INDEX NAME)

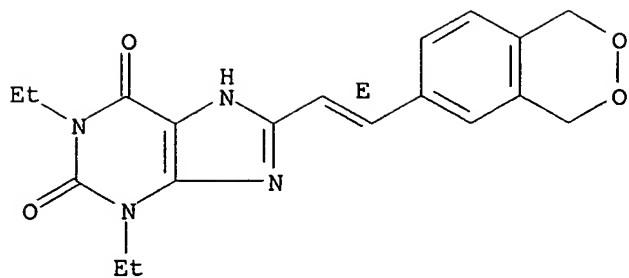
Double bond geometry as shown.



RN 155271-14-0 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,4-dihydro-2,3-benzodioxin-6-yl)ethenyl]-1,3-dihydro-, (E)- (9CI) (CA INDEX NAME)

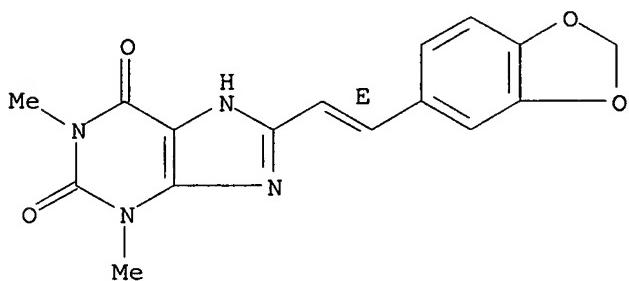
Double bond geometry as shown.



RN 155271-18-4 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-3,7-dihydro-1,3-dimethyl-, (E)- (9CI) (CA INDEX NAME)

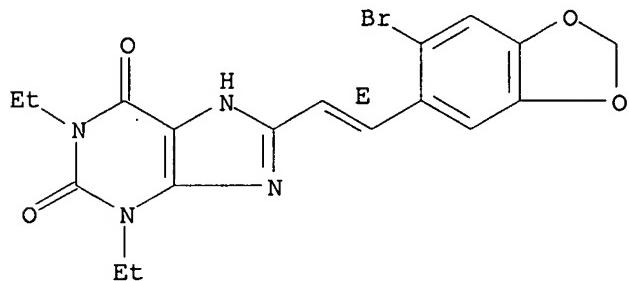
Double bond geometry as shown.



RN 155271-88-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(6-bromo-1,3-benzodioxol-5-yl)ethenyl]-1,3-diethyl-3,7-dihydro-, (E)- (9CI) (CA INDEX NAME)

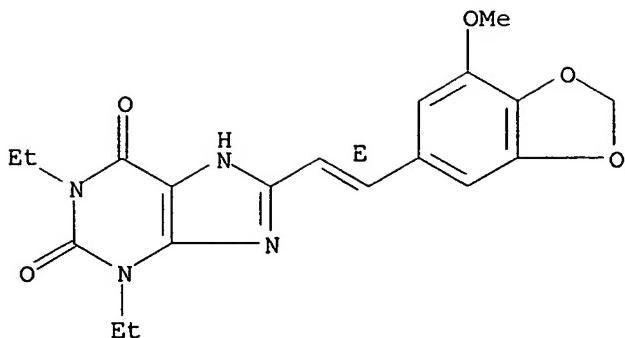
Double bond geometry as shown.



RN 155271-99-1 HCPLUS

CN 1H-Purine-2,6-dione, 1,3-diethyl-3,7-dihydro-8-[2-(7-methoxy-1,3-benzodioxol-5-yl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L5 ANSWER 65 OF 163 HCPLUS COPYRIGHT 2002 ACS

1994:217071 Document No. 120:217071 Photochemical reactions of caffeine with aliphatic aldehydes. Erndt, Aleksander; Fiedorowicz, Maciej; Kostuch, Andrzej; Para, Andrzej (Hugo Kollatay Univ. Agric., Krakow, 30-059, Pol.). Liebigs Annalen der Chemie (10), 1043-6 (English) 1993. CODEN: LACHDL. ISSN: 0170-2041.

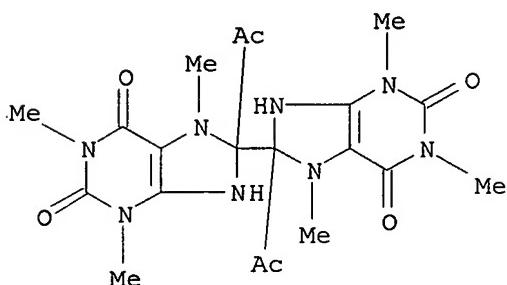
AB Photochem. reactions of caffeine with several aliph. aldehydes are performed. In the reactions with ethanal, propanal and butanal stable 8-acyl-8,9-dihydrocaffeines and their 8,8'-dimers were produced together with unreduced 8-acylcaffeines and 8-(.alpha.-hydroxyalkyl)caffeines. Under similar conditions, the reactions of 2-methylpropanal, 2-methylbutanal and 2,2-dimethylbutanal gave the 8-alkylcaffeines.

IT 154219-95-1P 154219-96-2P 154219-97-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

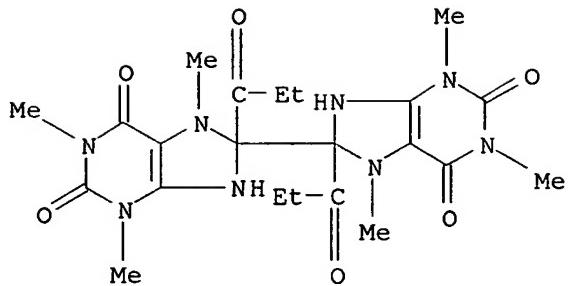
RN 154219-95-1 HCPLUS

CN [8,8'-Bi-1H-purine]-2,2',6,6'-tetrone, 8,8'-diacetyl-3,3',7,7',8,8',9,9'-octahydro-1,1',3,3',7,7'-hexamethyl- (9CI) (CA INDEX NAME)



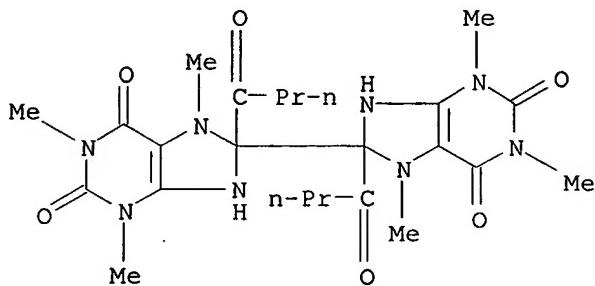
RN 154219-96-2 HCPLUS

CN [8,8'-Bi-1H-purine]-2,2',6,6'-tetrone, 3,3',7,7',8,8',9,9'-octahydro-1,1',3,3',7,7'-hexamethyl-8,8'-bis(1-oxopropyl)- (9CI) (CA INDEX NAME)



RN 154219-97-3 HCPLUS

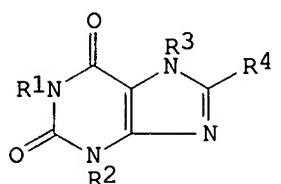
CN [8,8'-Bi-1H-purine]-2,2',6,6'-tetrone, 3,3',7,7',8,8',9,9'-octahydro-1,1',3,3',7,7'-hexamethyl-8,8'-bis(1-oxobutyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 66 OF 163 HCPLUS COPYRIGHT 2002 ACS

1994:144161 Document No. 120:144161 Pharmaceutical compositions containing xanthine derivatives for treatment of Parkinson's disease. Suzuki, Fumio; Shimada, Junichi; Ishii, Akio; Ichikawa, Shunji (Kyowa Hakko Kogyo Co., Ltd., Japan). Eur. Pat. Appl. EP 565377 A1 19931013, 49 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1993-302780 19930408. PRIORITY: JP 1992-87115 19920408.

GI



I

AB Pharmaceutical compns. contg. xanthine derivs. (I; R1, R2, R3=H, C1-6 alkyl or allyl; R4= C3-8 cycloalkyl) are useful for treatment of Parkinson's disease. (E)-6-amino-5-(3,4-dimethyoxyxycinnamoyl)amino-1,3-dipropyluracil (prepn. is given) was refluxed in NaOH soln., then was neutralized and the deposited crysts. were sepd. to obtain (E)-8-(3,4-dimethyoxyxstyryl)-1,3-dipropylxanthine (II). To II in DMF was

added K<sub>2</sub>CO<sub>3</sub> and MeI and the mixt. was heated at 50.degree. for 30min followed by filtration and addn. of water. The filtrate was extd. with CHCl<sub>3</sub> and the ext. was washed, dried, evapd., and purified to obtain (E)-8-(3,4-dimethoxystyryl)-7-methyl-1,3-dipropylxanthine (III). A tablet contained III 20, lactose 143.4, potato starch 30, hydroxypropyl cellulose 6, and Mg stearate 0.6mg.

IT 151539-58-1P 151539-61-6P

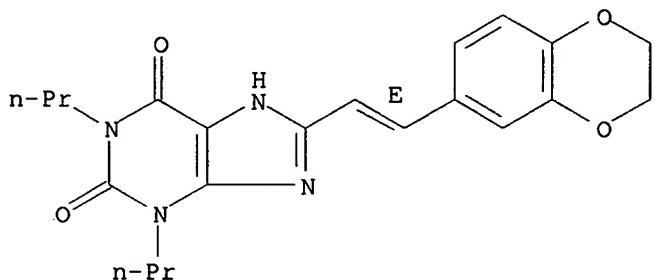
RL: PREP (Preparation)

(prepn. of, pharmaceutical compn. contg., for treatment of Parkinson's disease)

RN 151539-58-1 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(2,3-dihydro-1,4-benzodioxin-6-yl)ethenyl]-3,7-dihydro-1,3-dipropyl-, (E)- (9CI) (CA INDEX NAME)

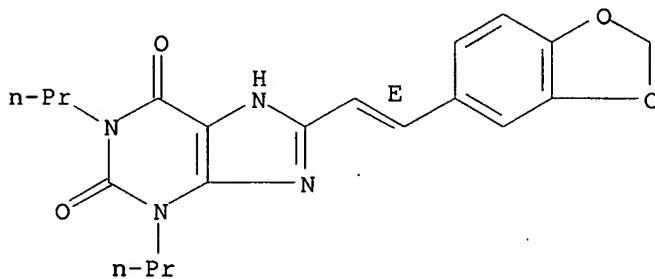
Double bond geometry as shown.



RN 151539-61-6 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(1,3-benzodioxol-5-yl)ethenyl]-3,7-dihydro-1,3-dipropyl-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



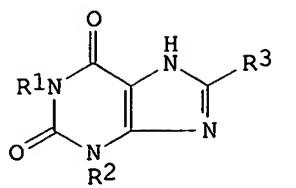
L5 ANSWER 67 OF 163 HCPLUS COPYRIGHT 2002 ACS

1993:662498 Document No. 119:262498 Substituted xanthines as tumor necrosis factor (TNF) inhibitors for the treatment of fungal and yeast infections. Esser, Klaus Max; Demarsh, Peter Lawrence; Frey, Carrie Lynn (SmithKline Beckman Corp., USA). PCT Int. Appl. WO 9316699 A1 19930902, 38 pp.

DESIGNATED STATES: W: AU, CA, JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2.

APPLICATION: WO 1993-US1496 19930219. PRIORITY: US 1992-839838 19920221.

GI



**AB** The title xanthine derivs. are I [R1, R2 = alkyl,  $(CH_2)mA$ , provided that  $.g \geq 1$  of R1 and R2 is  $(CH_2)mA$  ( $m = 0-3$ , A = (substituted) cyclic hydrocarbyl); R3 = halo, nitro, NR4R5 (R4, R5 = H, alkyl, alkylcarbonyl, or R4 and R5 together to the N to which they are attached form a (substituted) heterocyclyl)] and pharmaceutically acceptable salts thereof. 1,3-Dicyclopropylmethyl-8-aminoxanthine had an IC<sub>50</sub> of approx. 0.05  $\mu\text{M}$  in an in vitro TNF prodn. assay system. Formulations of I are included.

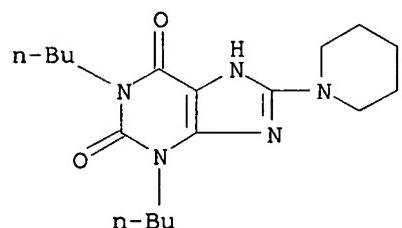
**IT** 132186-73-3 132186-74-4 132186-75-5  
132186-76-6 132186-77-7 132210-44-7

RL: BIOL (Biological study)

(for yeast or fungal infection treatment, TNF prodn. inhibition in relation to)

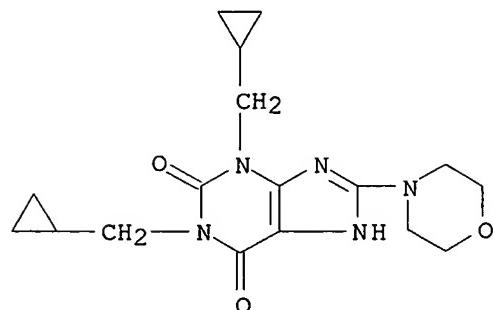
**RN** 132186-73-3 HCPLUS

**CN** 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



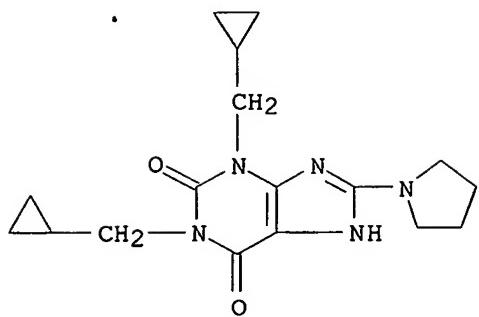
**RN** 132186-74-4 HCPLUS

**CN** 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(4-morpholinyl)- (9CI) (CA INDEX NAME)

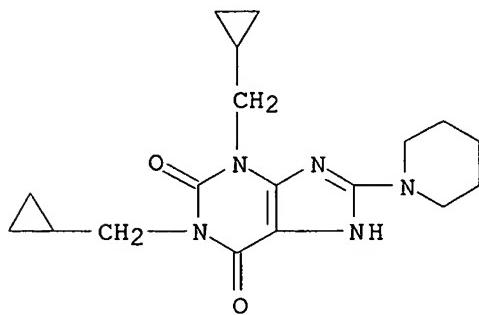


**RN** 132186-75-5 HCPLUS

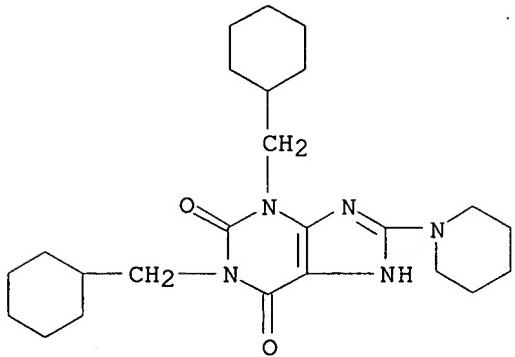
**CN** 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



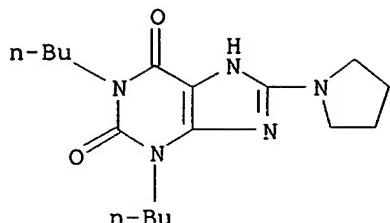
RN 132186-76-6 HCAPLUS  
CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



RN 132186-77-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 1,3-bis(cyclohexylmethyl)-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



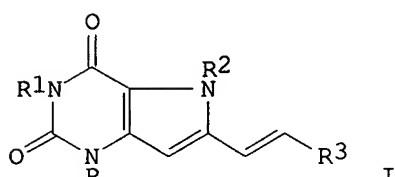
RN 132210-44-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 68 OF 163 HCPLUS COPYRIGHT 2002 ACS

1993:254617 Document No. 118:254617 Structure-activity relationships of 8-styrylxanthines as A2-selective adenosine antagonists. Jacobson, Kenneth A.; Gallo-Rodriguez, Carola; Melman, Neli; Fischer, Bilha; Maillard, Michel; van Bergen, Andrew; van Galen, Philip J. M.; Karton, Yishai (Lab. Bioorg. Chem., Natl. Inst. Diabet., Digest. Kidney Dis., Bethesda, MD, 20892, USA). Journal of Medicinal Chemistry, 36(10), 1333-42 (English) 1993. CODEN: JMCMAR. ISSN: 0022-2623.

GI



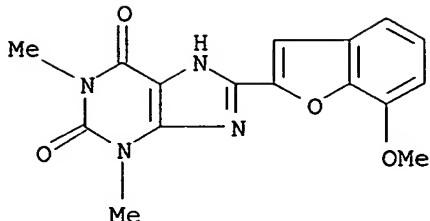
AB A series of substituted 8-styryl derivs. of 1,3,7-alkylxanthines I [i.e., R-R2 = H, Me, R3 = (un)substituted Ph] was synthesized as potential A2-selective adenosine receptor antagonists, and the potency at rat brain A1- and A2-receptors was studied in radioligand binding expts. At the xanthine 7-position, only small hydrophobic substituents were tolerated in receptor binding. 7-Me analogs were roughly 1 order of magnitude more selective for A2 vs. A1 receptors than the corresponding 7-H analogs. 1,3-Dimethylxanthine derivs. tended to be more selective for A2-receptors than the corresponding 1,3-diallyl, di-Et, or di-Pr derivs. Substitutions of the Ph ring at the 3-(monosubstituted) and 3,5-(disubstituted) positions were favored. I (R - R2 = Me, R3 = 3-ClC6H4) was a moderately potent and high A2-selective adenosine antagonist. I (R - R2 = Me, R3 = 3-HO2CCH2CH2CONHC6H4) was highly A2-selective and had enhanced water solv. I [R, R1 = Pr, R2 = Me, R3 = 3,5-(MeO)2C6H3] was a potent and very A2-selective adenosine antagonist.

IT 147700-56-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
(A2-selective adenosine antagonistic activity of)

RN 147700-56-9 HCPLUS

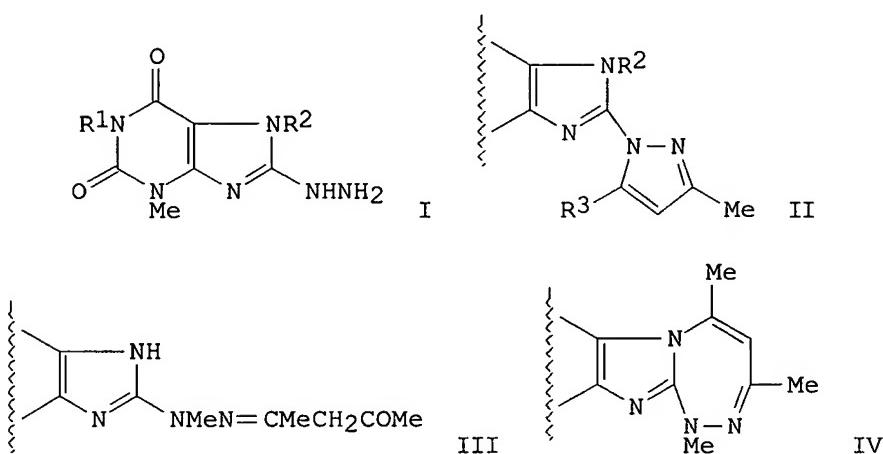
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(7-methoxy-2-benzofuranyl)-1,3-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 69 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1993:80706 Document No. 118:80706 Condensed imidazo-1,2,4-azines. XXVI. Reaction of 8-hydrazinoxanthines and 8-(1-methylhydrazino)theophylline with acetyl- and benzoylacetone. Povstyanoi, M. V.; Kruglenko, V. P.; Klyuev, N. A.; Aleksandrov, G. G.; Zakharkinskaya, E. V. (Kherson'sk. Ind. Inst., Kherson, Russia). Zhurnal Organicheskoi Khimii, 28(4), 849-56 (Russian) 1992. CODEN: ZORKAE. ISSN: 0514-7492.

GI



AB Reactions of purine bases I ( $R^1 = H, Me, R^2 = Me; R^1 = Me, R^2 = H$ ) with  $R^3CH_2COMe$  ( $R^3 = Ac, Bz$ ) gave 86-91% pyrazolylxanthines II whose structures ( $R^1 = H, R^2 = R^3 = Me$ ) were confirmed by x-ray anal. Sequential treatment of 8-bromotheophylline with  $MeNNH_2$  and  $MeCOCH_2COMe$  gave 49% hydrazone III which was heated to 170-175.degree. to give 55% triazenotheophylline IV.

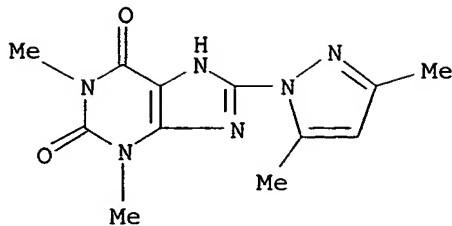
IT 145351-66-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and methylation of)

RN 145351-66-2 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(3,5-dimethyl-1H-pyrazol-1-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 70 OF 163 HCPLUS COPYRIGHT 2002 ACS

1992:511646 Document No. 117:111646 8-(acylamino)xanthines, a method for their preparation and their use as phosphodiesterase inhibitors, antiallergics, and for the treatment of eosinophilia. Buckle, Derek Richard; Smith, David Glynn; Fenwick, Ashley Edward (Beecham Group PLC, UK). PCT Int. Appl. WO 9205176 A1 19920402, 40 pp. DESIGNATED STATES: W: AU, CA, JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-GB1634 19910923. PRIORITY: GB 1990-20921 19900926.

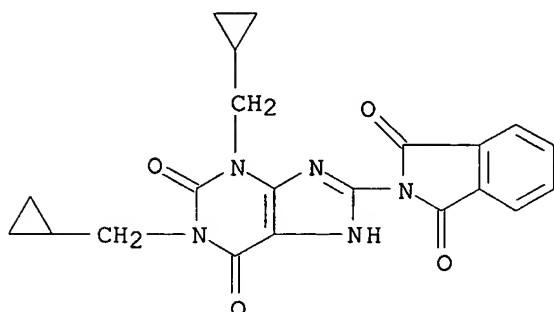
AB Certain 8-(acylamino)xanthine derivs. [8-(acylamino)-1H-purine-2,6-diones] are claimed. A process for their prepn. comprises the condensation reaction of 8-aminoxanthines with an anhydrides compd. The use of said compds. for the treatment of disorders assocd. with increased nos. of eosinophils (such as asthma), allergies assocd. with atopy is claimed; the compds. are phosphodiesterase inhibitors. Said compds. are also of potential use as tumor necrosis factor inhibitors or HIV inhibitors, or treatment of cognitive dysfunctions (no data). Treatment of 8-amino-1,3-bis(cyclopropylmethyl)xanthine with phthalic anhydride in Et3N/THF gave 1,3-bis(cyclopropylmethyl)-8-(phthalimido)xanthine (I) in 26% yield. I had activity in the treatment of blood eosinophilia in rats and as phosphodiesterase inhibitor.

IT 143095-01-6P, 1,3-Bis(cyclopropylmethyl)-8-phthalimidoxanthine  
143095-03-8P, 1,3-Bis(cyclopropylmethyl)-8-succinimidoxanthine

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, a phosphodiesterase inhibitor, antiallergic and for treatment of eosinophilia and)

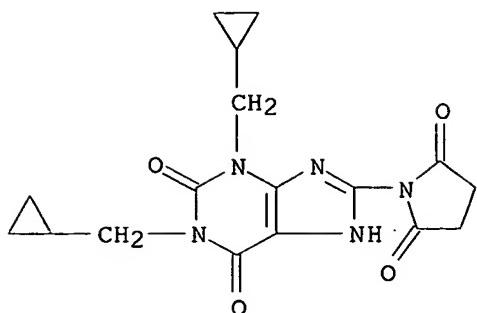
RN 143095-01-6 HCPLUS

CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-8-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-3,7-dihydro- (9CI) (CA INDEX NAME)



RN 143095-03-8 HCPLUS

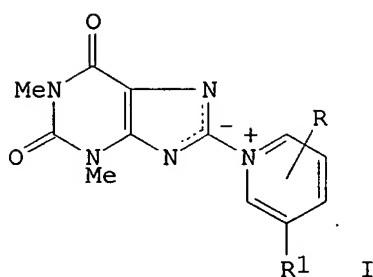
CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-8-(2,5-dioxo-1-pyrrolidinyl)-3,7-dihydro- (9CI) (CA INDEX NAME)..



L5 ANSWER 71 OF 163 HCPLUS COPYRIGHT 2002 ACS

1992:511561 Document No. 117:111561 A new method for the production of 8-pyridiniotheophyllinates. Bobkov, V. N.; Zvolinskaya, T. V.; Kuz'menko, I. I. (Kiev. Inst. Farmakol. Toksikol., Kiev, 252057, Ukraine). Khimiya Geterotsiklicheskikh Soedinenii (11), 1535-8 (Russian) 1991. CODEN: KGSSAQ. ISSN: 0453-8234.

GI



AB Title compds. I (R = H, 2-Me, 3-Me, 4-Me, R1 = H; R = 3-Me, R1 = Me) were prepd. by reaction of theophylline or 8-bromotheophylline with pyridines in the presence of an oxidizing agent, esp. chloramine-B.

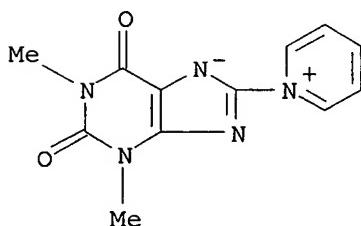
IT 52943-89-2P 142954-88-9P 142954-89-0P

142954-90-3P 142954-91-4P

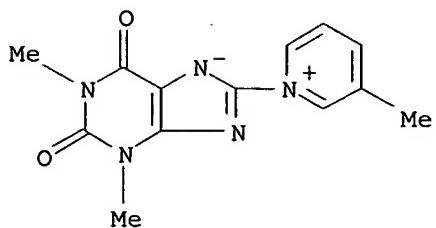
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 52943-89-2 HCPLUS

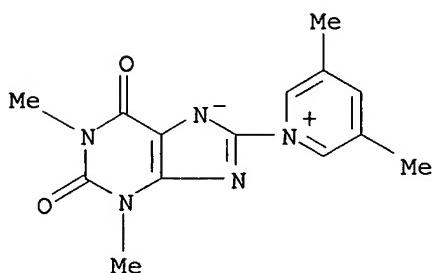
CN Pyridinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



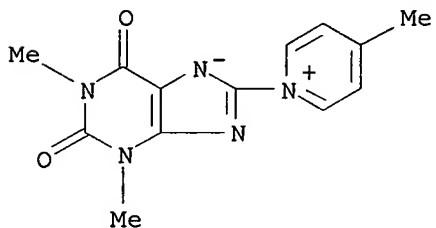
RN 142954-88-9 HCAPLUS  
CN Pyridinium, 3-methyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



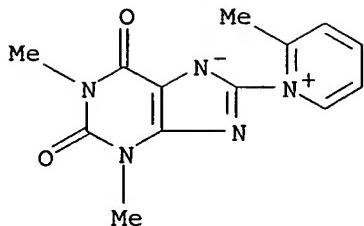
RN 142954-89-0 HCAPLUS  
CN Pyridinium, 3,5-dimethyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



RN 142954-90-3 HCAPLUS  
CN Pyridinium, 4-methyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



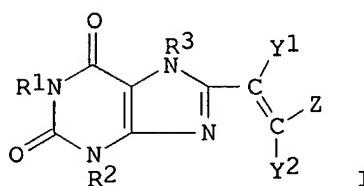
RN 142954-91-4 HCAPLUS  
CN Pyridinium, 2-methyl-1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



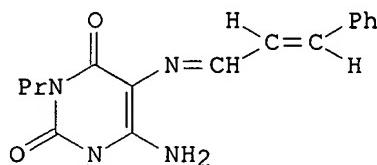
L5 ANSWER 72 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1992:490312 Document No. 117:90312 Preparation of xanthine derivatives as antiasthmatics and agents for treating osteoporosis. Suzuki, Fumio; Shimada, Junichi; Ishii, Akio; Nonaka, Hiromi; Kosaka, Nobuo; Ichikawa, Shunji (Kyowa Hakko Kogyo Co., Ltd., Japan). PCT Int. Appl. WO 9206976 A1 19920430, 48 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1991-JP1420 19911017. PRIORITY: JP 1990-280171 19901018.

GI



I



II

AB Xanthine derivs. [I, R<sup>1</sup>, R<sup>2</sup> = H, Pr, Bu, allyl; R<sup>3</sup> = H, alkyl; Y<sup>1</sup>, Y<sup>2</sup> = H, Me, Z = (substituted) Ph, pyridyl, imidazolyl, furyl, thiienyl], effective adenosine antagonists, are prepd. and formulated. Condensation reaction of cinnamaldehyde with 5,6-diamino-1,3-dipropyluracil in MeOH-HOAc gave 70% enamine II, which was refluxed with FeCl<sub>3</sub> in EtOH to give 61% (E)-I (R<sup>1</sup> = R<sup>2</sup> = Pr, R<sup>3</sup> = Y<sup>1</sup> = Y<sup>2</sup> = H, Z = Ph) (III). Methylation of III with MeI in DMF gave 84% (E)-I (R<sup>3</sup> = Me, others remain unchanged) which showed 82% inhibition of adenosine A<sub>1</sub> receptor and 96% inhibition of A<sub>2</sub> receptor at 10<sup>-4</sup> M. I also showed 119% inhibition of bone absorption.

IT 142665-23-4P 142665-24-5P

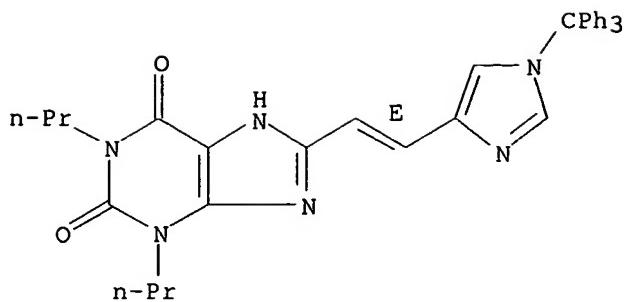
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prep<sup>n</sup>. and reaction of, in prep<sup>n</sup>. of adenosine antagonist)

RN 142665-23-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-[2-[1-(triphenylmethyl)-1H-imidazol-4-yl]ethenyl]-, (E)- (9CI) (CA INDEX NAME)

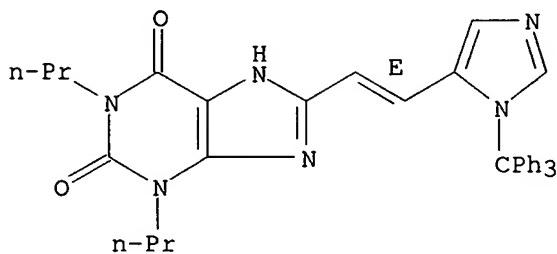
Double bond geometry as shown.



RN 142665-24-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-[2-[1-(triphenylmethyl)-1H-imidazol-5-yl]ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



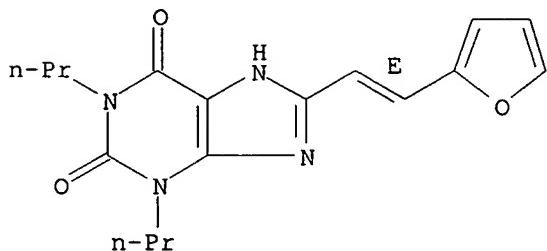
IT 142665-27-8P 142665-29-0P 142665-32-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of, as antiasthmatic and antiosteoporosis agent)

RN 142665-27-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-(2-furanyl)ethenyl]-3,7-dihydro-1,3-dipropyl-, (E)- (9CI) (CA INDEX NAME)

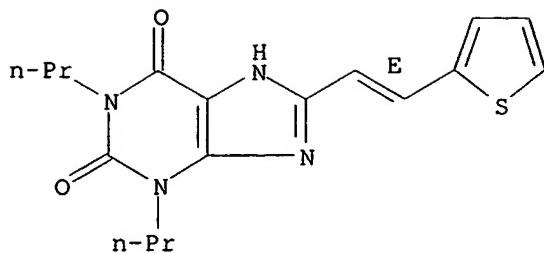
Double bond geometry as shown.



RN 142665-29-0 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-[2-(2-thienyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

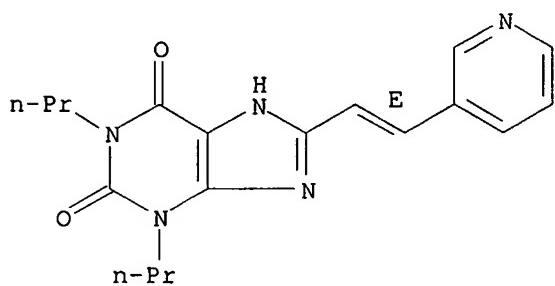
Double bond geometry as shown.



RN 142665-32-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-[2-(3-pyridinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L5 ANSWER 73 OF 163 HCPLUS COPYRIGHT 2002 ACS

1992:462998 Document No. 117:62998 8-substituted xanthines as tumor necrosis factor (TNF) inhibitors. Esser, Klaus Max (SmithKline Beckman Corp., USA). PCT Int. Appl. WO 9209203 A1 19920611, 35 pp. DESIGNATED STATES: W: AU, CA, HU, JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US8734 19911120. PRIORITY: US 1990-616479 19901121.

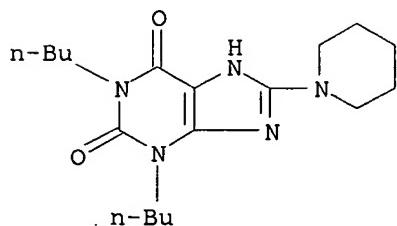
AB 8-Substituted xanthines are useful as tumor necrosis factor (TNF) inhibitors. TNF prodn. by human monocytes was inhibited in vitro by 1,3-dicyclopropylmethyl-8-aminoxanthine; the IC50 was 0.05 .mu.M. Various formulation examples are presented.

IT 132186-73-3 132186-74-4 132186-75-5  
132186-76-6 132186-77-7 132210-44-7

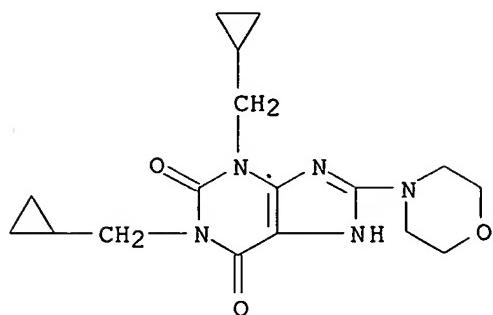
RL: BIOL (Biological study)  
(as tumor necrosis factor inhibitor, pharmaceutical compn. contg.)

RN 132186-73-3 HCPLUS

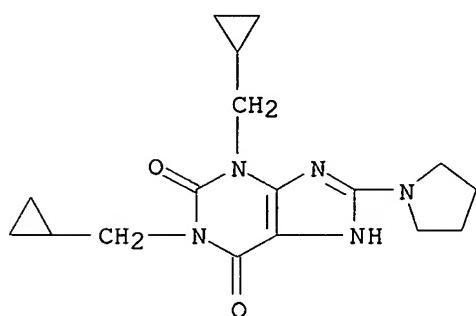
CN 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



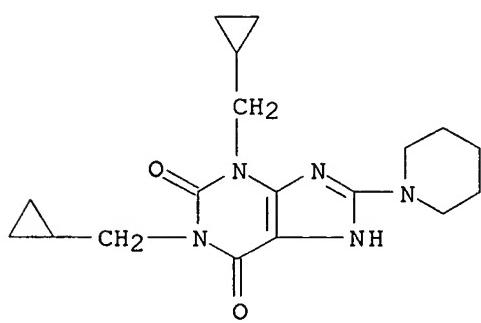
RN 132186-74-4 HCAPLUS  
CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(4-morpholinyl)- (9CI) (CA INDEX NAME)



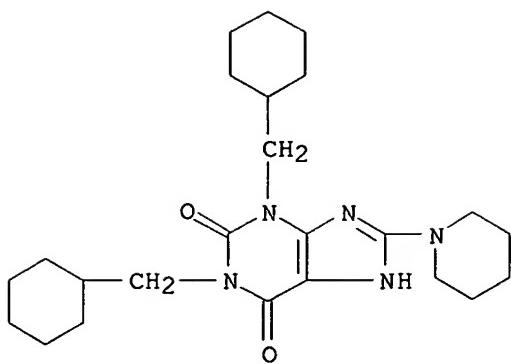
RN 132186-75-5 HCAPLUS  
CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 132186-76-6 HCAPLUS  
CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)

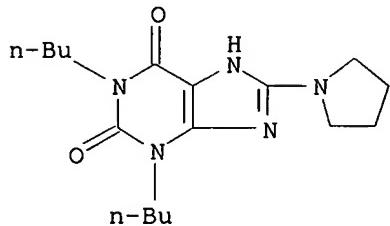


RN 132186-77-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 1,3-bis(cyclohexylmethyl)-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



RN 132210-44-7 HCPLUS

CN 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-(1-pyrrolidinyl)- (9CI)  
(CA INDEX NAME)



L5 ANSWER 74 OF 163 HCPLUS COPYRIGHT 2002 ACS

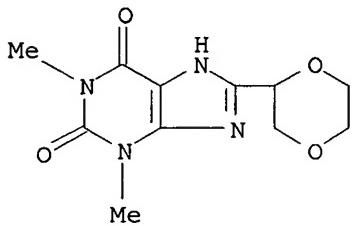
1992:458570 Document No. 117:58570 Photochemistry of purine systems. Part V. Photochemical reactions of theophylline with alcohols and ethers initiated by 254 nm UV radiation. Erndt, Aleksander; Kostuch, Andrzej; Para, Andrzej; Fiedorowicz, Maciej (Dep. Chem. Phys., Agric. Univ., Krakow, 30-059, Pol.). Universitatis Iagellonicae Acta Chimica, 35, 83-7 (English) 1991. CODEN: UIACEG. ISSN: 0867-1095.

AB Photochem. reactions of theophylline with aliph. alcs. and dialkyl and cyclic ethers initiated by 254 nm radiation result in substitution of the hydrogen atom at C-8 position. A free-radical mechanism is proposed for these reactions and the quantum yields of products formation are estd.

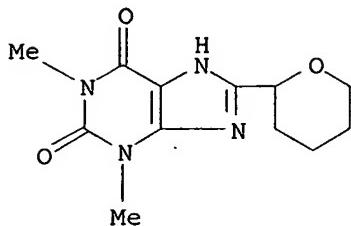
IT 66274-13-3P 66274-14-4P 66274-15-5P  
RL: FORM (Formation, nonpreparative); PREP (Preparation)  
(formation of, in photosubstitution reaction of theophylline)

RN 66274-13-3 HCPLUS

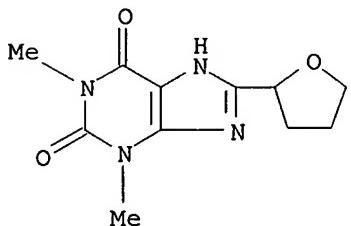
CN 1H-Purine-2,6-dione, 8-(1,4-dioxan-2-yl)-3,7-dihydro-1,3-dimethyl- (9CI)  
(CA INDEX NAME)



RN 66274-14-4 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2H-pyran-2-yl)-  
(9CI) (CA INDEX NAME)

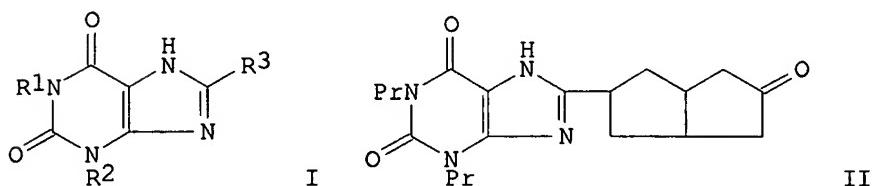


RN 66274-15-5 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2-furanyl)-  
(9CI) (CA INDEX NAME)



L5 ANSWER 75 OF 163 HCPLUS COPYRIGHT 2002 ACS  
1992:426198 Document No. 117:26198 Preparation of [(poly)cyclic  
(oxa)alkyl]xanthines and analogs as adenosine antagonists. Kuefner-Muehl,  
Ulrike; Stransky, Werner; Walther, Gerhard; Weber, Karl Heinz; Ensinger,  
Helmut; Kuhn, Franz Josef; Schingnitz, Guenter; Lehr, Erich (Boehringer  
Ingelheim K.-G., Germany). Ger. Offen. DE 4019892 A1 19920102, 28 pp.  
(German). CODEN: GWXXBX. APPLICATION: DE 1990-4019892 19900622.

GI



AB Title compds. [I; R1, R2 = alkyl, alkenyl, alkynyl; R3 = N-attached heterocyclyl, monosaccharide, cycloalkanone ketal; (poly)cyclic (oxa)alkyl, etc.] were prep'd. as adenosine antagonists (no data). Thus, 7-carboxyspiro[cis-bicyclo[3.3.0]octane-3,2'-(1,3-dithiolane)] (prepn. given) was cyclocondensed with 5,6-diamino-1,3-dipropyluracil and the product hydrolyzed to give title compd. II.

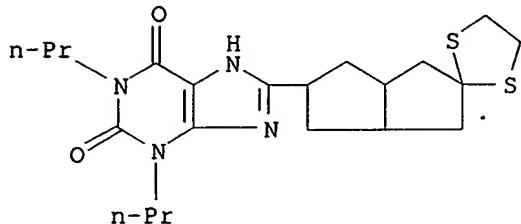
IT 141283-34-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, in prepn. of adenosine antagonists)

RN 141283-34-3 HCPLUS

CN 1H-Purine-2,6-dione, 8-(hexahydrospiro[1,3-dithiolane-2,2'(1'H)-pentalen]-5'-yl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



IT 127946-21-8P 141283-17-2P 141283-20-7P

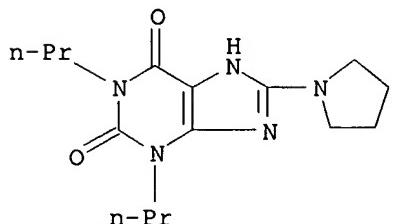
141283-21-8P 141283-23-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as adenosine antagonist)

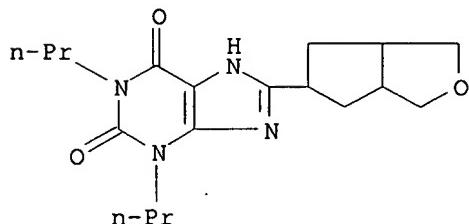
RN 127946-21-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



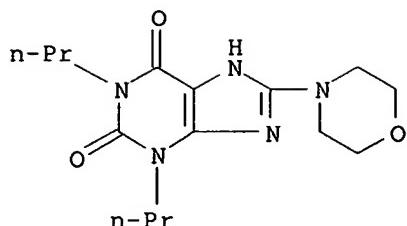
RN 141283-17-2 HCPLUS

CN 1H-Purine-2,6-dione, 8-(hexahydro-1H-cyclopenta[c]furan-5-yl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 141283-20-7 HCPLUS

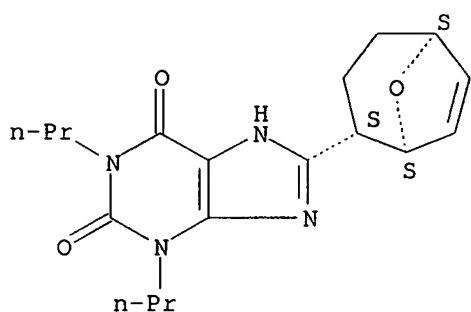
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-morpholinyl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 141283-21-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(8-oxabicyclo[3.2.1]oct-6-en-2-yl)-1,3-dipropyl-, exo- (9CI) (CA INDEX NAME)

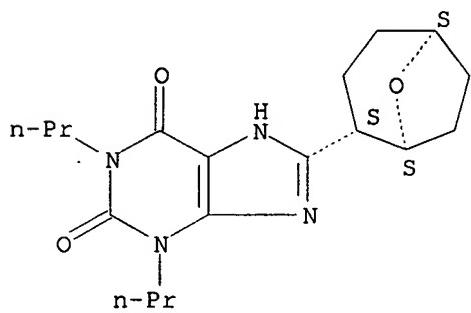
Relative stereochemistry.



RN 141283-23-0 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(8-oxabicyclo[3.2.1]oct-2-yl)-1,3-dipropyl-, exo- (9CI) (CA INDEX NAME)

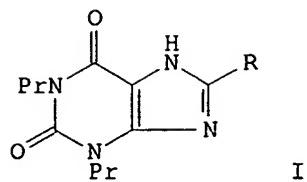
Relative stereochemistry.



L5 ANSWER 76 OF 163 HCPLUS COPYRIGHT 2002 ACS

1992:187478 Document No. 116:187478 8-Polycycloalkyl-1,3-dipropylxanthines as potent and selective antagonists for Al-adenosine receptors. Shimada, Junichi; Suzuki, Fumio; Nonaka, Hiromi; Ishii, Akio (Pharm. Res. Lab., Kyowa Hakko Kogyo Co., Ltd., 411, Japan). Journal of Medicinal Chemistry, 35(5), 924-30 (English) 1992. CODEN: JMCMAR. ISSN: 0022-2623.

GI



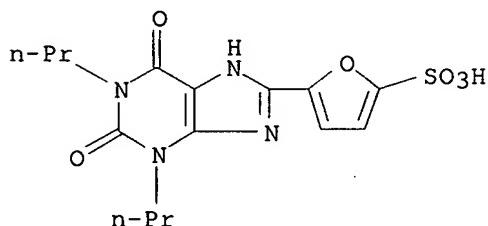
AB With the aim of characterizing the hydrophobic interactions between xanthines and the A1 receptor site, 1,3-dipropyl-8-substituted xanthines (I, R = e.g., heteraryl, alkyl, alicyclic, or noradamantyl group) were prepd. Introduction of a quaternary carbon and the conformationally restricted cyclopental moiety into the 8-position of xanthine enhanced the adenosine A1 antagonism. 1,3-Dipropyl-8-(3-noradamantyl)xanthine was identified to be a selective and the most potent A1 receptor antagonist reported to date. Under the structure-activity relation study, the 8-substituent of xanthine antagonists and the N6-substituent of adenosine agonists appears to bind to the same region of the A1 receptor.

IT **140437-59-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 140437-59-8 HCAPLUS

CN 2-Furansulfonic acid, 5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-, monopotassium salt (9CI) (CA INDEX NAME)



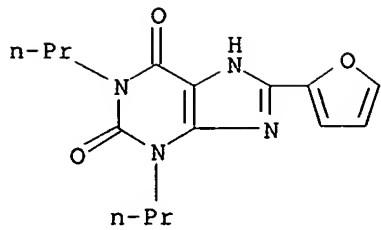
● K

IT **117027-86-8P 121542-93-6P 136198-98-6P  
136198-99-7P 139348-59-7P 139348-60-0P  
139348-61-1P 139348-62-2P 139348-63-3P  
139348-64-4P 139348-65-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of and adenosine A1 and A2 receptor binding by)

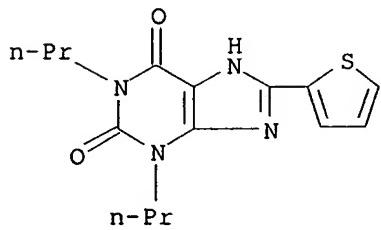
RN 117027-86-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



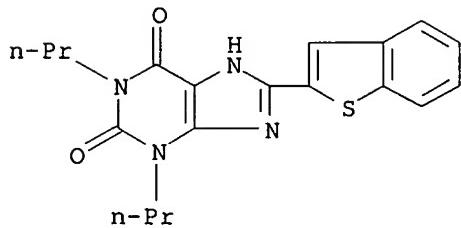
RN 121542-93-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



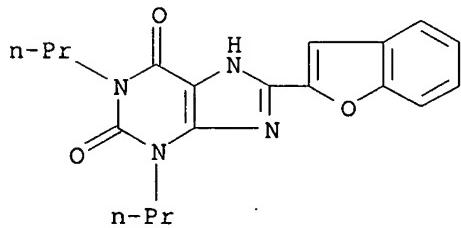
RN 136198-98-6 HCAPLUS

CN 1H-Purine-2,6-dione, 8-benzo[b]thien-2-yl-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



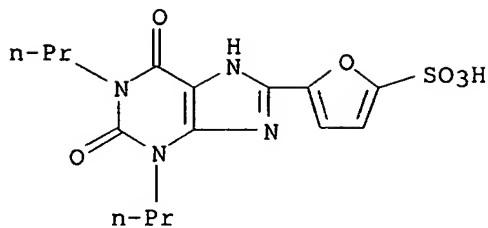
RN 136198-99-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-benzofuranyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)

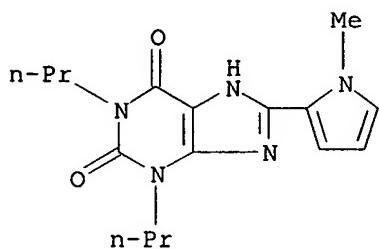


RN 139348-59-7 HCAPLUS

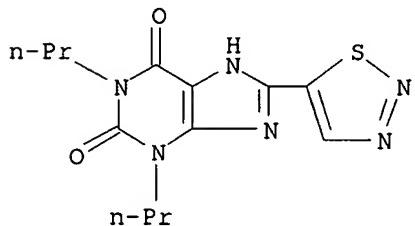
CN 2-Furansulfonic acid, 5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



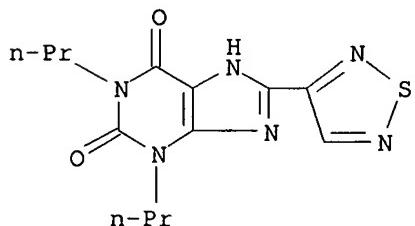
RN 139348-60-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-methyl-1H-pyrrol-2-yl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



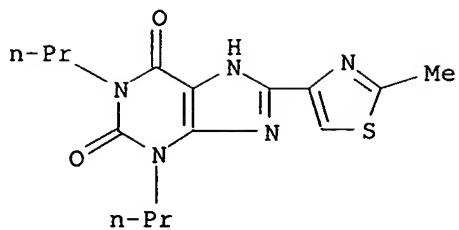
RN 139348-61-1 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(1,2,3-thiadiazol-5-yl)- (9CI) (CA INDEX NAME)



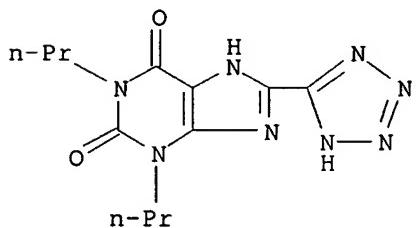
RN 139348-62-2 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(1,2,5-thiadiazol-3-yl)- (9CI) (CA INDEX NAME)



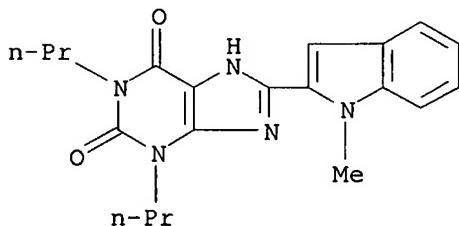
RN 139348-63-3 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(2-methyl-4-thiazolyl)-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 139348-64-4 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(1H-tetrazol-5-yl)- (9CI)  
 (CA INDEX NAME)



RN 139348-65-5 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-methyl-1H-indol-2-yl)-1,3-dipropyl- (9CI)  
 (CA INDEX NAME)



L5 ANSWER 77 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1992:151416 Document No. 116:151416 1,3,8-Trisubstituted xanthines. Effects of substitution pattern upon adenosine receptor A1/A2 affinity [Erratum to document cited in CA114(19):185119j]. Erickson, Ronald H.; Hiner, Roger N.; Feeney, Scott W.; Blake, Paul R.; Rzeszotarski, Waclaw J.; Hicks, Rickey P.; Costello, Diane G.; Abreu, Mary E. (Nova Pharm. Corp., Baltimore, MD, 21224, USA). Journal of Medicinal Chemistry, 34(12), 3405 (English) 1991. CODEN: JMCMAR. ISSN: 0022-2623.

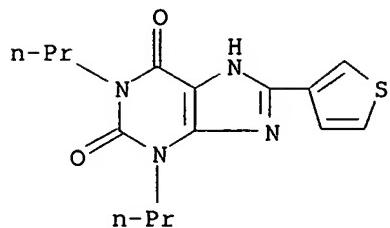
AB An error in ref. 18 has been cor. The error was not reflected in the abstr. or the index entries.

IT 117027-85-7P 121542-93-6P 132940-25-1P  
 132940-26-2P 132940-27-3P 132940-28-4P  
 132940-29-5P 132940-30-8P 132940-31-9P  
 132940-32-0P 132940-33-1P 132940-34-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and adenosine receptor binding affinity of (Erratum))

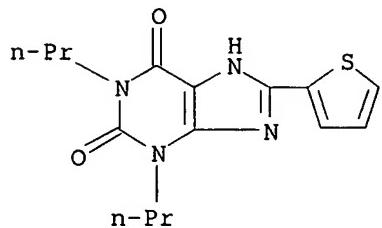
RN 117027-85-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



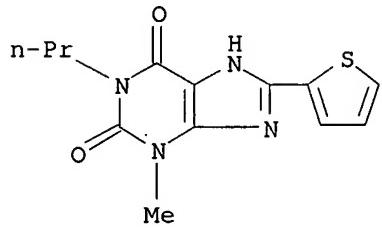
RN 121542-93-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



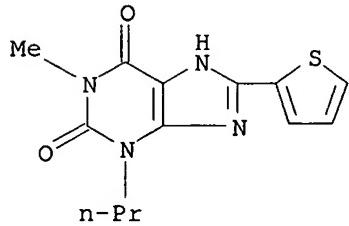
RN 132940-25-1 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-propyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



RN 132940-26-2 HCPLUS

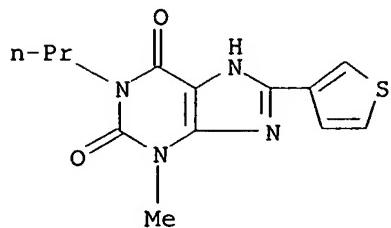
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-propyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



RN 132940-27-3 HCPLUS

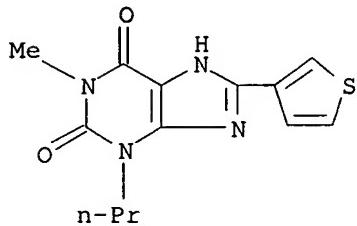
Searched by: Mary Hale 308-4258 CM-1 1E01

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-propyl-8-(3-thienyl)- (9CI)  
(CA INDEX NAME)



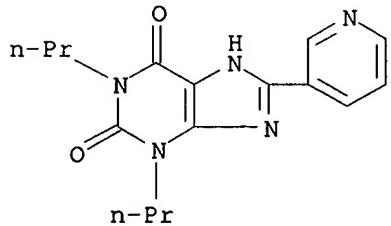
RN 132940-28-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-propyl-8-(3-thienyl)- (9CI)  
(CA INDEX NAME)



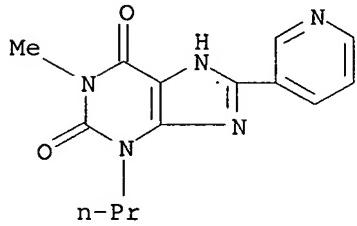
RN 132940-29-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-pyridinyl)- (9CI) (CA  
INDEX NAME)



RN 132940-30-8 HCPLUS

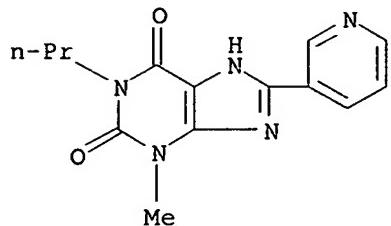
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-propyl-8-(3-pyridinyl)- (9CI)  
(CA INDEX NAME)



RN 132940-31-9 HCPLUS

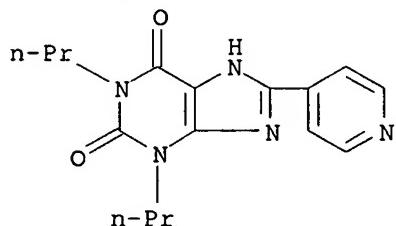
Searched by: Mary Hale 308-4258 CM-1 1E01

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-propyl-8-(3-pyridinyl)- (9CI)  
(CA INDEX NAME)



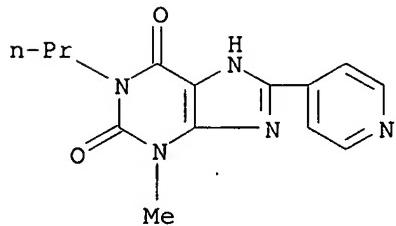
RN 132940-32-0 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



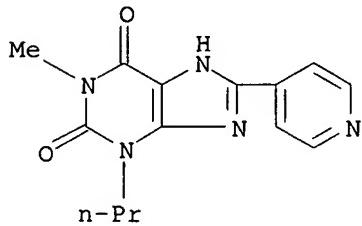
RN 132940-33-1 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-propyl-8-(4-pyridinyl)- (9CI)  
(CA INDEX NAME)



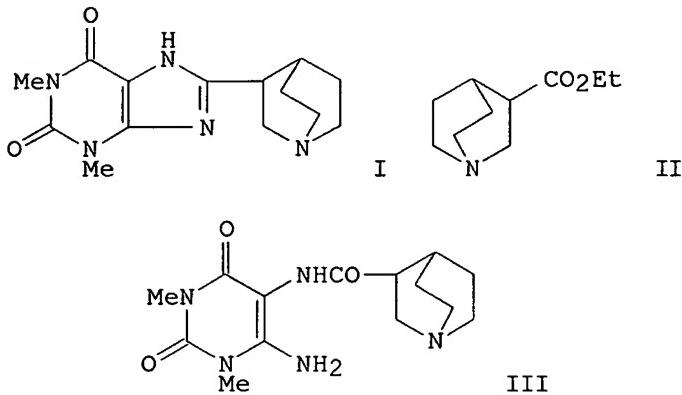
RN 132940-34-2 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-propyl-8-(4-pyridinyl)- (9CI)  
(CA INDEX NAME)

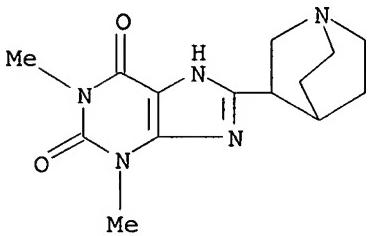


L5 ANSWER 78 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1991:632164 Document No. 115:232164 Synthesis and study of  
 1,3-dimethyl-8-(quinuclidyl-31)xanthine. Zhikhareva, G. P.; Yakhontov, L.  
 N.; Marshalkin, M. F.; Turchin, K. F.; Kuleshova, E. F.; Sheinker, Yu. N.  
 (TSKhLS, VNIKhFI, Moscow, USSR). Khimiko-Farmatsevticheskii Zhurnal,  
 25(1), 32-6 (Russian) 1991. CODEN: KHFZAN. ISSN: 0023-1134. OTHER  
 SOURCES: CASREACT 115:232164.

GI

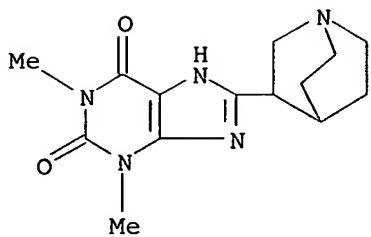


AB The title compd. I was prep'd. from quinuclidinecarboxylate II in 4 steps via uracil III. The biol. activity of I was studied.  
 IT 134580-22-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep'n. of)  
 RN 134580-22-6 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-(1-azabicyclo[2.2.2]oct-3-yl)-3,7-dihydro-1,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

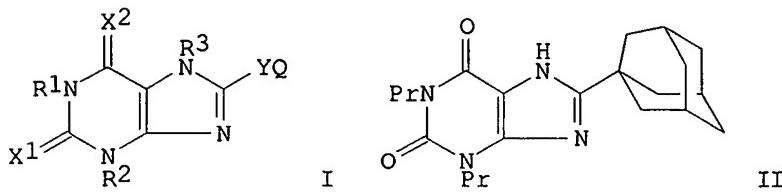
IT 134580-19-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep'n., toxicity and cardiotonic activity of)  
 RN 134580-19-1 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-(1-azabicyclo[2.2.2]oct-3-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 79 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1991:558836 Document No. 115:158836 Préparation and formulation of 8-(polycycloalkyl)xanthines and analogs as adenosine A<sub>1</sub> receptor antagonists. Suzuki, Fumio; Shimada, Junichi; Ishii, Akio; Ohno, Tetsuji; Karasawa, Akira; Kubo, Kazuhiro; Nonaka, Hiromi (Kyowa Hakko Kogyo Co., Ltd., Japan). Eur. Pat. Appl. EP 415456 A2 19910306, 45 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-116791 19900831. PRIORITY: JP 1989-226642 19890901.

GI



AB The title compds. [I; Q = norbornyl, pentalenyl, adamantyl, (un)substituted pyridyl, thiazolyl, etc.; R1-R3 = H, alkyl; Y = bond, alkylene; X1, X2 = O, S] were prep'd. Thus, 3-noradamantanecarboxylic acid was treated with SOC12 in pyridine after which 1,3-dipropyl-5,6-diaminouracil was added and stirring continued to give 6-amino-5-(noradamantane-3-carbonylamino)-1,3-dipropyluracil which was heated with POC13 to give title compd. II. The latter gave 315% increase in urine output (Na<sup>+</sup>/K<sup>+</sup> = 2.05) in rats receiving 25 mg/kg orally.

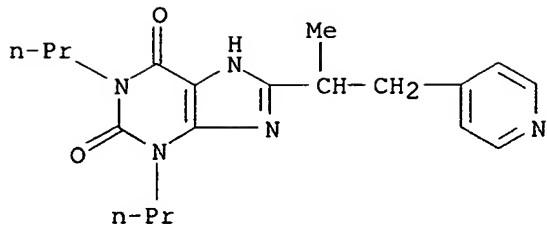
IT 136198-96-4P 136198-97-5P 136198-98-6P

136198-99-7P 136199-01-4P

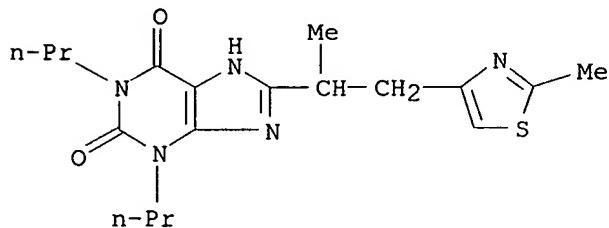
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of, as adenosine A<sub>1</sub> receptor antagonist)

RN 136198-96-4 HCAPLUS

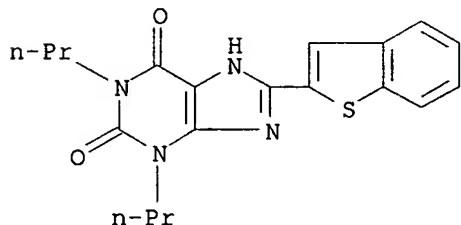
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[1-methyl-2-(4-pyridinyl)ethyl]-1,3-dipropyl- (9CI) (CA INDEX NAME)



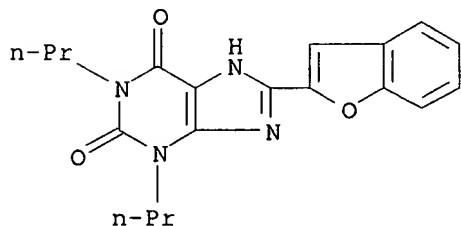
RN 136198-97-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[1-methyl-2-(2-methyl-4-thiazolyl)ethyl]-1,3-dipropyl- (9CI) (CA INDEX NAME)



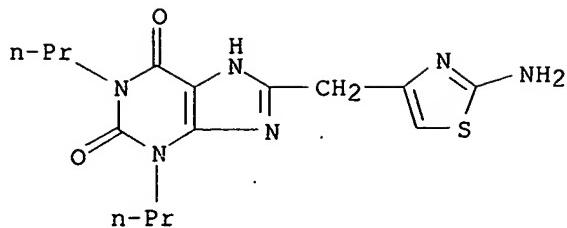
RN 136198-98-6 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-benzo[b]thien-2-yl-3,7-dihydro-1,3-dipropyl- (9CI)  
 (CA INDEX NAME)



RN 136198-99-7 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-(2-benzofuranyl)-3,7-dihydro-1,3-dipropyl- (9CI)  
 (CA INDEX NAME)



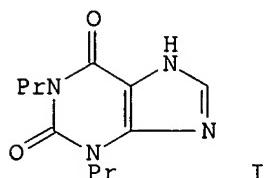
RN 136199-01-4 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(2-amino-4-thiazolyl)methyl]-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



L5 ANSWER 80 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1991:549734 Document No. 115:149734 Mapping the xanthine C8-region of the adenosine A1 receptor with computer graphics. Van der Wenden, Eleonora M.; Van Galen, Philip J. M.; Ijzerman, Adriann P.; Soudijn, Willem (Div. Med. Chem., Cent. Bio-Pharm. Sci., Leiden, 2300 RA, Neth.). European Journal of Pharmacology, Molecular Pharmacology Section, 206(4), 315-23 (English) 1991. CODEN: EJPPEF. ISSN: 0922-4106.

GI



AB Substitution at the 8-position of 1,3-dipropylxanthines (I) can lead to very potent and selective adenosine A1 antagonists. The xanthine C8-region was investigated using computer-assisted mol. modeling. This region can be divided into two subregions with a considerable overlap in vol.: a Ph region which binds the flat substituents and a cycloalkyl region which binds the other substituents. The 8-phenyl-substituted derivs. bind with an N9-C8-C1'-C2' dihedral angle of 220.degree.; this dihedral angle is 330.degree. for the 8-cycloalkyl-substituted derivs. The lower affinity of C8-substituted 7-methyl-1,3-dipropylxanthines can be explained quant. with steric hindrance, which C8-substituents experience from the 7-Me group in these conformations. The substitution pattern dets. the affinity for 8-phenyl-substituted compds. for which the energy cost to reach the dihedral angle of 220.degree. is low, but has little influence otherwise. The affinity of the 8-cycloalkyl-1,3-dipropylxanthines is mainly vol.-dependent, because of a forbidden area near the cycloalkyl region.

IT 108653-57-2 108653-58-3 108653-59-4  
112683-71-3 117027-85-7 117027-86-8

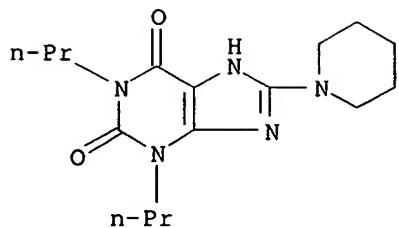
121542-93-6

RL: BIOL (Biological study)

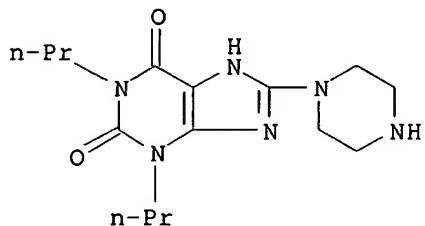
(brain adenosine A1 receptors interaction with, structure in relation to)

RN 108653-57-2 HCAPLUS

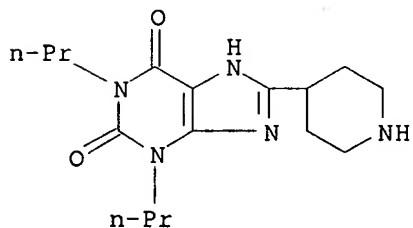
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



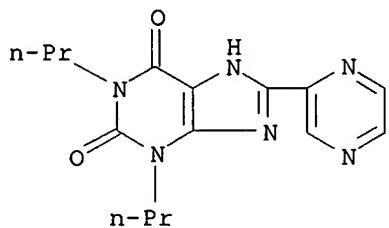
RN 108653-58-3 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-piperazinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



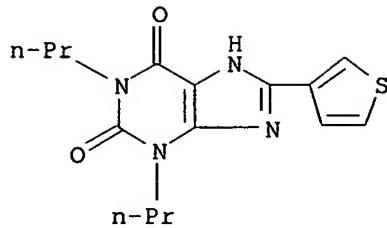
RN 108653-59-4 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



RN 112683-71-3 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-pyrazinyl- (9CI) (CA INDEX NAME)

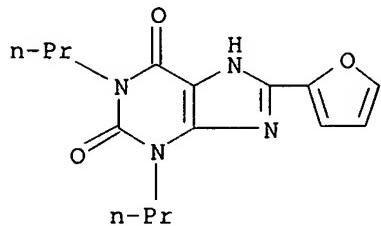


RN 117027-85-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



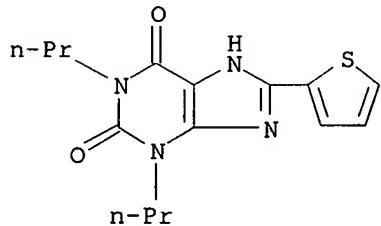
RN 117027-86-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 121542-93-6 HCPLUS

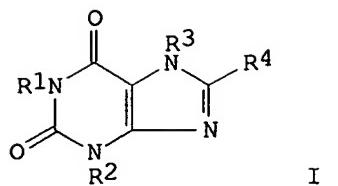
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 81 OF 163 HCPLUS COPYRIGHT 2002 ACS

1991:519847 Document No. 115:119847 Utilization of xanthines, optionally incorporated in liposomes, to stimulate the pigmentation of skin or hair. Bonte, Frederic; Dumas, Marc; Meybeck, Alain; Marechal, Christian (LVMH Recherche, Fr.). PCT Int. Appl. WO 9107945 A1 19910613, 39 pp. DESIGNATED STATES: W: AU, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (French). CODEN: PIXXD2. APPLICATION: WO 1990-FR822 19901116. PRIORITY: FR 1989-15653 19891128.

GI



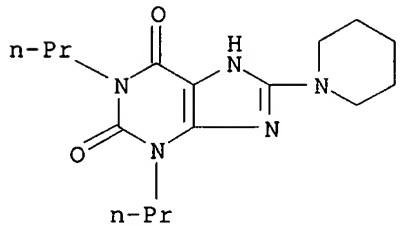
AB The xanthines I [R<sub>1</sub>R<sub>2</sub> = H, alkyl, alkenyl, alkynyl, aralkyl, etc.; R<sub>3</sub> = H, (un)substituted alkyl, benzyl; R<sub>4</sub> = H, halo, alkyl, aryl, (un)substituted NH<sub>2</sub>, etc.] stimulate hair and skin pigmentation to reinforce the natural defenses of the skin against solar radiation. I are preferably incorporated into liposomes. 3-Isobutyl-1-methylxanthine (0.2 g) was incorporated, as usual, into liposomes made of 3.6 g lecithin and 0.4 g .beta.-sitosterol. The liposomes, applied to the skin of guinea pigs, prior to UV irradn., stimulated melanogenesis, *in vivo*.

IT 108653-57-2

RL: BIOL (Biological study)  
(hair and skin pigmentation stimulation by)

RN 108653-57-2 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)

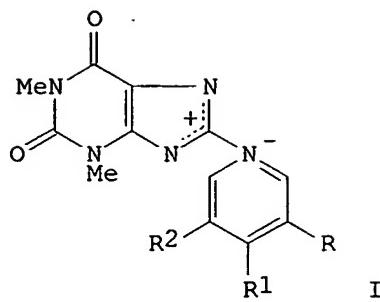


L5 ANSWER 82 OF 163 HCPLUS COPYRIGHT 2002 ACS

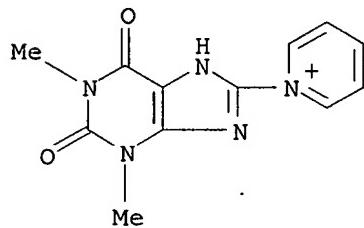
1991:206871 Document No. 114:206871 Reaction of 8-bromotheophylline with pyridine and alkylpyridines. 8-Pyridiniotheophyllinates. Bobkov, V. N.; Zvolinskaya, T. V.; Kuz'menko, I. I. (Kiev. Nauchno-Issled. Inst. Farmakol. Toksikol., Kiev, 252057, USSR). Khimiya Geterotsiklicheskikh Soedinenii (11), 1541-4 (Russian) 1990. CODEN: KGSSAQ. ISSN: 0453-8234.

OTHER SOURCES: CASREACT 114:206871.

GI

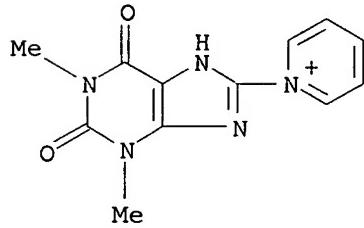


- AB The title reaction gives ylides I ( $R, R_1, R_2 = H, Me$ ). Acid catalysis by  $(PhO)_2POCl$  or  $Ac_2O$  improves the yield of I from 11% to 80-90%. The mechanism of this reaction is discussed.
- IT 133513-00-5P 133513-01-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)
- RN 133513-00-5 HCAPLUS
- CN Pyridinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, chloride (9CI) (CA INDEX NAME)



●  $Cl^-$

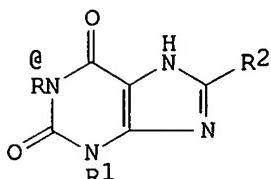
- RN 133513-01-6 HCAPLUS
- CN Pyridinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, bromide (9CI) (CA INDEX NAME)



●  $Br^-$

1991:185119 Document No. 114:185119 1,3,8-Trisubstituted xanthines. Effects of substitution pattern upon adenosine receptor A1/A2 affinity. Erickson, Ronald H.; Hiner, Roger N.; Feeney, Scott W.; Blake, Paul R.; Rzeszotarski, Waclaw J.; Hicks, Rickey P.; Costello, Diane G.; Abreu, Mary E. (Nova Pharm. Corp., Baltimore, MD, 21224, USA). Journal of Medicinal Chemistry, 34(4), 1431-5 (English) 1991. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 114:185119.

GI



I

AB The title compds. I (R, R1 = Me, Pr; R2 = Ph, 4-HOC<sub>6</sub>H<sub>4</sub>, 4-NCC<sub>6</sub>H<sub>4</sub>, PhCH<sub>2</sub>CH<sub>2</sub>, PhCH:CH, 2-thienyl, 3-pyridyl, 4-pyridyl, cyclopentyl, cyclohexyl) were prep'd. and were assessed for affinity and selectivity in binding to adenosine A1 and A2 receptors. I (R = R1 = Pr) had the greatest affinity at the A1 receptor. With one exception, these compds. also exhibited the most potent binding at the A2 receptor; however, I (R = Me, R1 = Pr) were equipotent with I (R = R1 = Pr) at the A2 receptor. Addnl., the substituents on the 1- and 3-positions of I were equally important for detg. max. affinity to the A1 receptor, while the substituent at the 3-position is more important than the substituent at the 1-position for potency at the A2 receptor. As a result, it is possible to maximize selectivity for the A1 receptor by choice of the 1- and 3-position substituents. However, the substitution pattern required for max. A1 selectivity is also dependent upon the substituent in the 8-position in a manner which is not fully understood.

IT 117027-85-7P 121542-93-6P 132940-25-1P

132940-26-2P 132940-27-3P 132940-28-4P

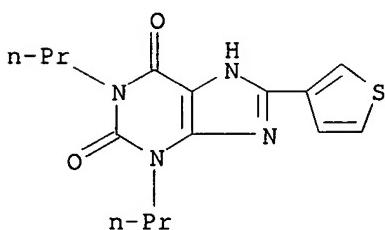
132940-29-5P 132940-30-8P 132940-31-9P

132940-32-0P 132940-33-1P 132940-34-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and adenosine receptor binding affinity of)

RN 117027-85-7 HCPLUS

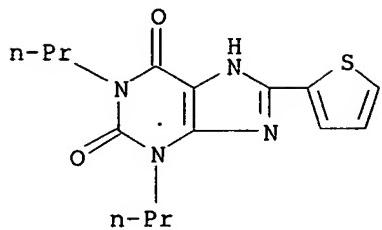
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



RN 121542-93-6 HCPLUS

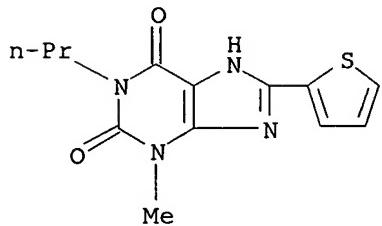
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(2-thienyl)- (9CI) (CA

INDEX NAME)



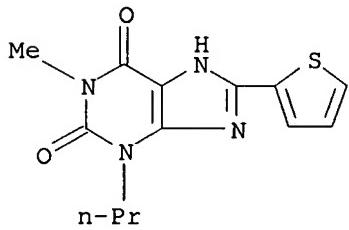
RN 132940-25-1 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-propyl-8-(2-thienyl)- (9CI)  
(CA INDEX NAME)



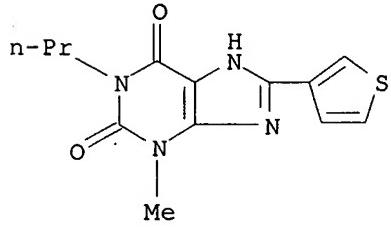
RN 132940-26-2 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-propyl-8-(2-thienyl)- (9CI)  
(CA INDEX NAME)



RN 132940-27-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-propyl-8-(3-thienyl)- (9CI)  
(CA INDEX NAME)

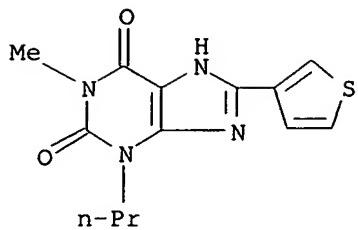


RN 132940-28-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-propyl-8-(3-thienyl)- (9CI)

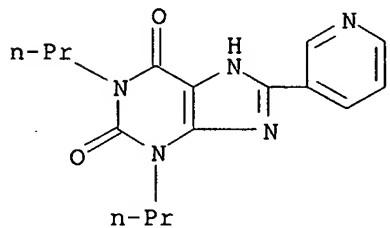
Searched by: Mary Hale 308-4258 CM-1 1E01

(CA INDEX NAME)



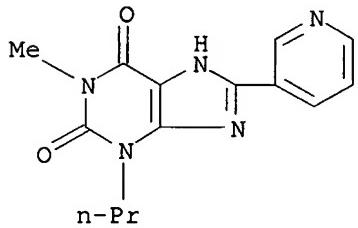
RN 132940-29-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



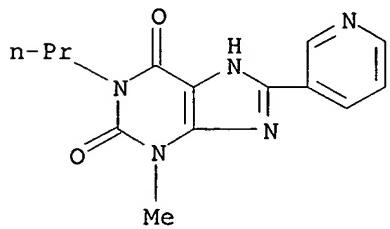
RN 132940-30-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-propyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 132940-31-9 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-propyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)

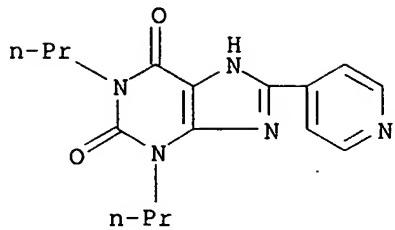


RN 132940-32-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)

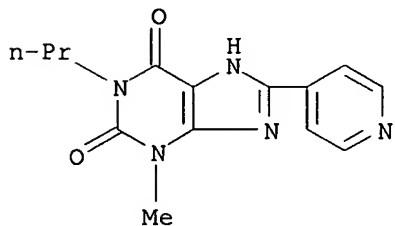
Searched by: Mary Hale 308-4258 CM-1 1E01

INDEX NAME)



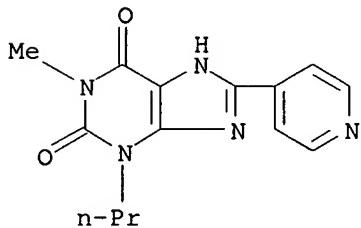
RN 132940-33-1 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-1-propyl-8-(4-pyridinyl)- (9CI)  
(CA INDEX NAME)



RN 132940-34-2 HCPLUS

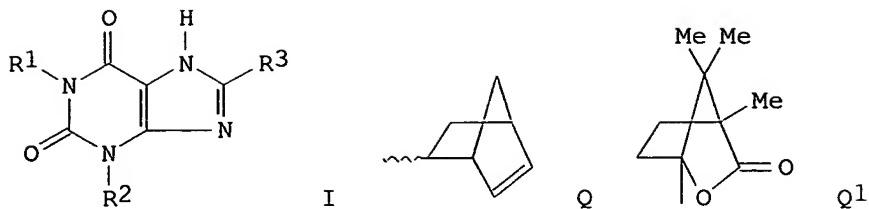
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-propyl-8-(4-pyridinyl)- (9CI)  
(CA INDEX NAME)



L5 ANSWER 84 OF 163 HCPLUS COPYRIGHT 2002 ACS

1991:164265 Document No. 114:164265 Preparation of xanthines as adenosine antagonists. Kuefner-Muehl, Ulrike; Weber, Karl Heinz; Walther, Gerhard; Stransky, Werner; Ensinger, Helmut; Schingnitz, Guenter; Kuhn, Franz Josef; Lehr, Erich (Boehringer Ingelheim K.-G., Germany). Ger. Offen. DE 3843117 A1 19900628, 20 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1988-3843117 19881222.

GI



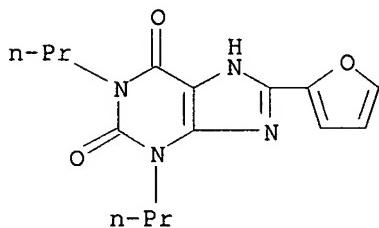
**AB** The title compds. [I; R1 = C1-6 alkyl, C3-4 alkenyl or alkynyl; R2 = H, C1-6 alkyl, C3-4 alkenyl or alkynyl, (un)substituted benzyl; R3 = C-attached (un)satd. 5-, 6-, or 7-membered heterocycle contg. .gtoreq.1 O, S, and optionally substituted by C1-6 alkyl, CHO, CH<sub>2</sub>OR<sub>4</sub>, CO<sub>2</sub>R<sub>4</sub>, CONR<sub>5</sub>R<sub>6</sub>, etc., C4-8 cycloalkyl, (un)substituted C3-8 cycloalkane, (un)substituted C4-8 cycloalkanone or cycloalkanol, C<sub>6</sub>H<sub>3</sub>R<sub>7</sub>R<sub>8</sub>-3,4, fluorenyl, bicyclyl residues Q, Q<sub>1</sub>, etc.; R<sub>4</sub> = H, C1-13 alkyl, propargyl, etc.; R<sub>5</sub> = H, C1-6 alkyl, etc.; R<sub>6</sub> = H, C1-6 alkyl, PhCH<sub>2</sub>, etc.; R<sub>7</sub>R<sub>8</sub> = OCH<sub>2</sub>O, OCH<sub>2</sub>CH<sub>2</sub>O] and their pharmacol. unobjectionable salts, adenosine antagonists having a specific affinity for the A<sub>1</sub> receptor-subtype, useful for the treatment of the ageing-related illnesses, e.g., senile dementia and Alzheimer's disease, were prep'd. A soln. of 2.9 g 1-benzyl-3-propyl-5-nitroso-6-aminouracil, prep'd. by N-propylation of 1-benzyl-6-aminouracil followed by nitrosation, and 2.3 g 1,4-benzodioxane-6-aldehyde in DMF was treated with 0.5 g Me<sub>2</sub>NNH<sub>2</sub> and the mixt. was refluxed 8 h to give 1 g I (R<sub>1</sub> = PhCH<sub>2</sub>, R<sub>2</sub> = Pr, R<sub>3</sub> = 1,4-benzodioxin-6-yl). The K<sub>i</sub> of 9 I for the adenosine A<sub>1</sub> receptor were 2 .times. 10<sup>-9</sup> to 8 .times. 10<sup>-9</sup> nM and >1 .times. 10<sup>-5</sup> to 9 .times. 10<sup>-5</sup> nM for the A<sub>2</sub> receptor.

**IT** 117027-86-8

RL: RCT (Reactant); RACT (Reactant or reagent)  
(Vilsmeier formylation of, in prepn. of adenosine antagonist)

**RN** 117027-86-8 HCPLUS

**CN** 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)

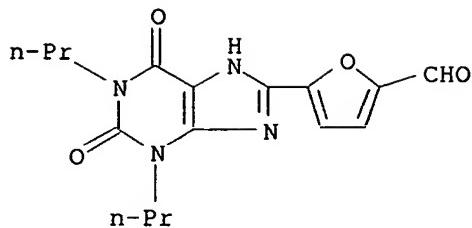


**IT** 133058-43-2

RL: RCT (Reactant); RACT (Reactant or reagent)  
(oxidn. of, in prepn. of adenosine antagonist)

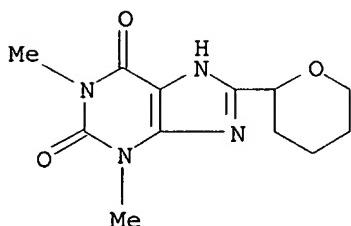
**RN** 133058-43-2 HCPLUS

**CN** 2-Furancarboxaldehyde, 5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)

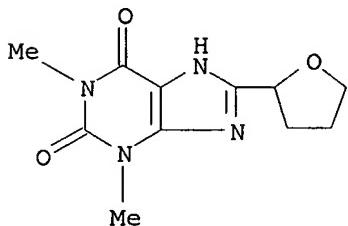


IT 66274-14-4P 66274-15-5P 117027-80-2P  
 117027-81-3P 117027-85-7P 117027-86-8P  
 121542-93-6P 133058-39-6P 133058-40-9P  
 133058-41-0P 133058-42-1P 133058-43-2P  
 133058-44-3P 133058-45-4P 133058-46-5P  
 133058-51-2P 133058-52-3P 133058-53-4P  
 133058-54-5P 133058-56-7P 133058-57-8P  
 133058-58-9P 133058-59-0P 133058-60-3P  
 133058-63-6P 133058-64-7P 133058-65-8P  
 133058-66-9P 133058-71-6P 133058-84-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. of, as adenosine antagonist)

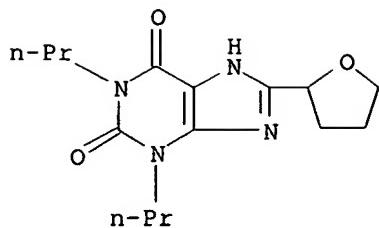
RN 66274-14-4 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2H-pyran-2-yl)-  
 (9CI) (CA INDEX NAME)



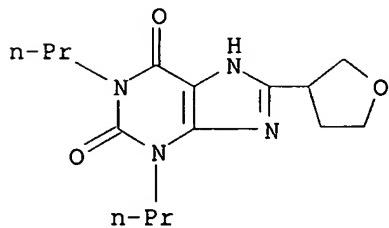
RN 66274-15-5 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2-furanyl)-  
 (9CI) (CA INDEX NAME)



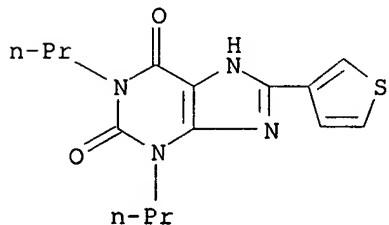
RN 117027-80-2 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(tetrahydro-2-furanyl)-  
 (9CI) (CA INDEX NAME)



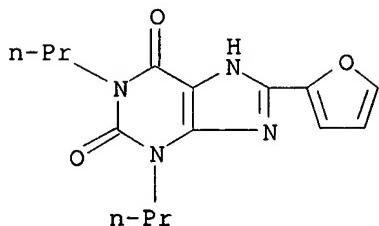
RN 117027-81-3 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(tetrahydro-3-furanyl)- (9CI) (CA INDEX NAME)



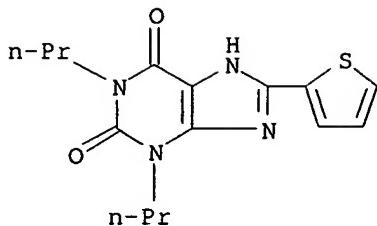
RN 117027-85-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



RN 117027-86-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)

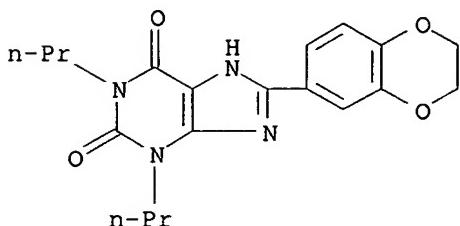


RN 121542-93-6 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



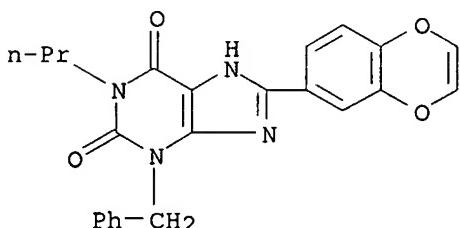
RN 133058-39-6 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2,3-dihydro-1,4-benzodioxin-6-yl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



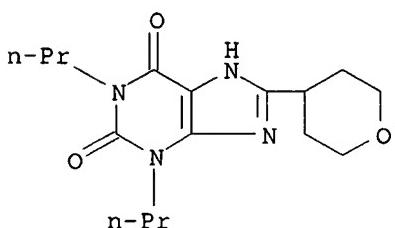
RN 133058-40-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(1,4-benzodioxin-6-yl)-3,7-dihydro-3-(phenylmethyl)-1-propyl- (9CI) (CA INDEX NAME)



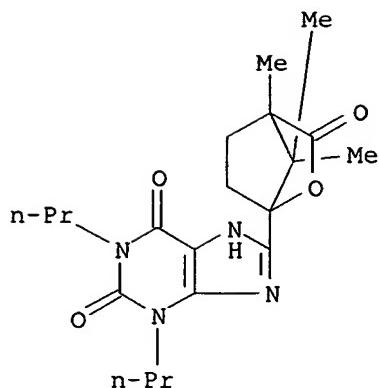
RN 133058-41-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(tetrahydro-2H-pyran-4-yl)- (9CI) (CA INDEX NAME)

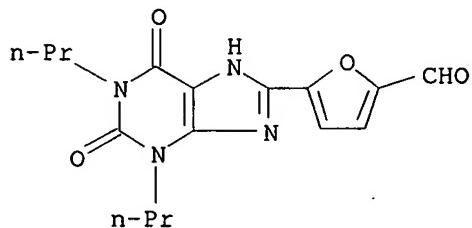


RN 133058-42-1 HCAPLUS

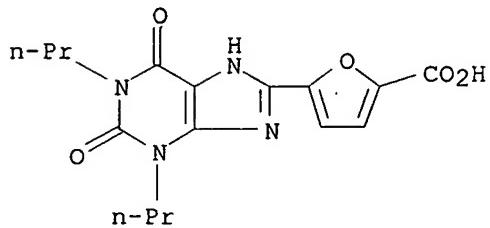
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]hept-1-yl)- (9CI) (CA INDEX NAME)



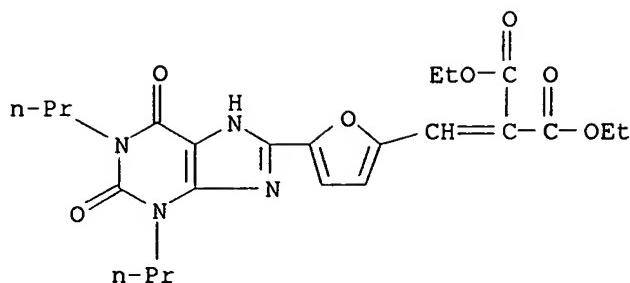
RN 133058-43-2 HCAPLUS  
 CN 2-Furancarboxaldehyde, 5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



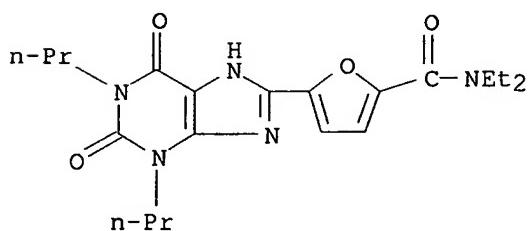
RN 133058-44-3 HCAPLUS  
 CN 2-Furancarboxylic acid, 5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



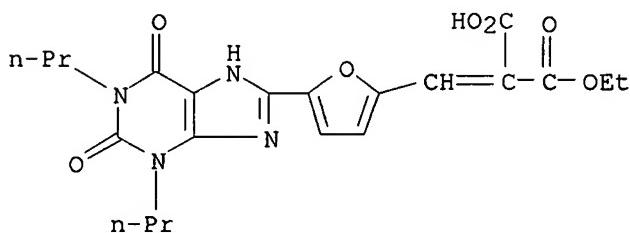
RN 133058-45-4 HCAPLUS  
 CN Propanedioic acid, {[5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-2-furanyl]methylene]-, diethyl ester (9CI) (CA INDEX NAME)



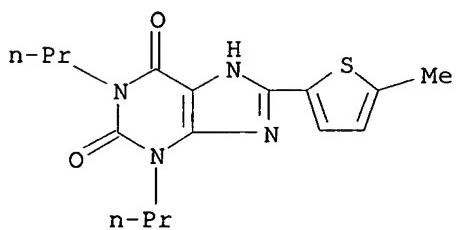
RN 133058-46-5 HCAPLUS  
 CN 2-Furancarboxamide, N,N-diethyl-5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



RN 133058-51-2 HCAPLUS  
 CN Propanedioic acid, [5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-2-furanyl]methylene]-, monoethyl ester (9CI) (CA INDEX NAME)

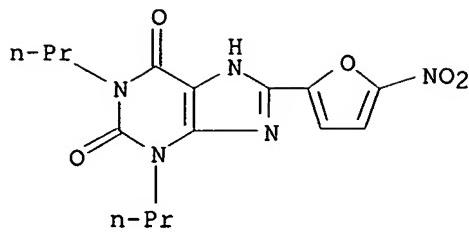


RN 133058-52-3 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(5-methyl-2-thienyl)-1,3-dipropyl- (9CI) (CA INDEX NAME)

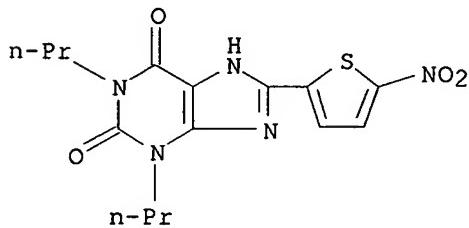


RN 133058-53-4 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(5-nitro-2-furanyl)-1,3-dipropyl- (9CI)

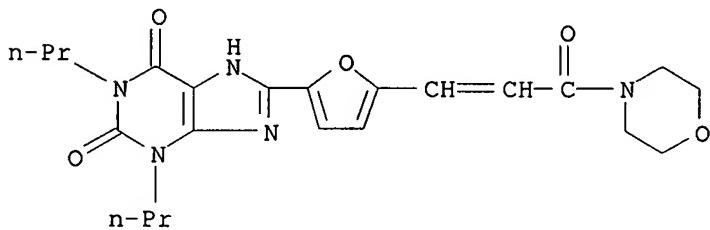
(CA INDEX NAME)



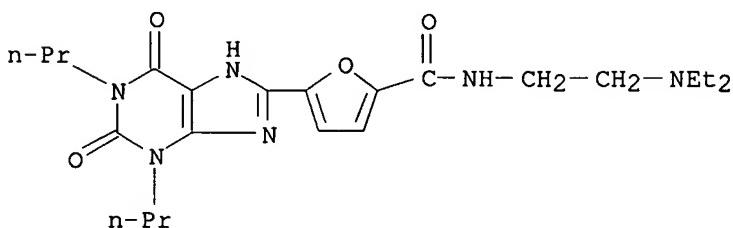
RN 133058-54-5 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(5-nitro-2-thienyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



RN 133058-56-7 HCPLUS  
CN Morpholine, 4-[1-oxo-3-[5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-2-furanyl]-2-propenyl]- (9CI) (CA INDEX NAME)

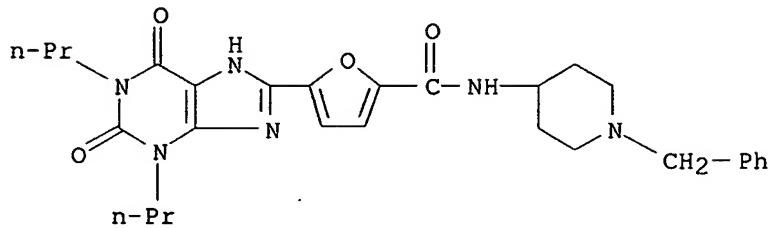


RN 133058-57-8 HCPLUS  
CN 2-Furancarboxamide, N-[2-(diethylamino)ethyl]-5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



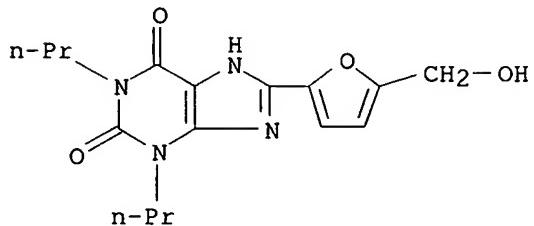
RN 133058-58-9 HCPLUS  
CN 2-Furancarboxamide, N-[1-(phenylmethyl)-4-piperidinyl]-5-(2,3,6,7-

tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



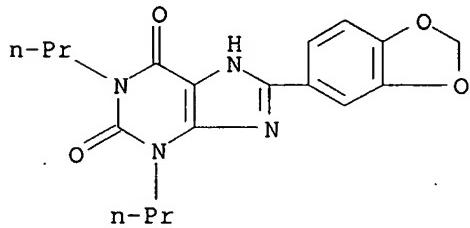
RN 133058-59-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[5-(hydroxymethyl)-2-furanyl]-1,3-dipropyl- (9CI) (CA INDEX NAME)



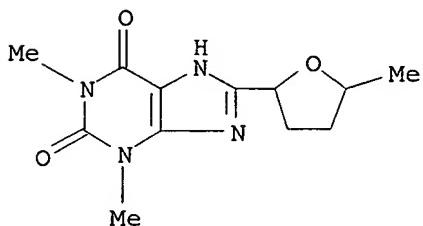
RN 133058-60-3 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(1,3-benzodioxol-5-yl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 133058-63-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-5-methyl-2-furanyl)- (9CI) (CA INDEX NAME)

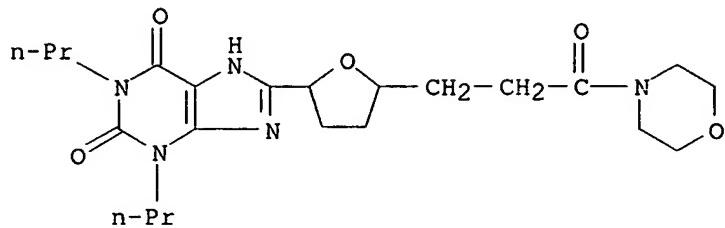


RN 133058-64-7 HCAPLUS

CN Morpholine, 4-[1-oxo-3-[tetrahydro-5-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dimethyl-1H-purin-8-yl)methyl]propyl]methyl- (9CI) (CA INDEX NAME)

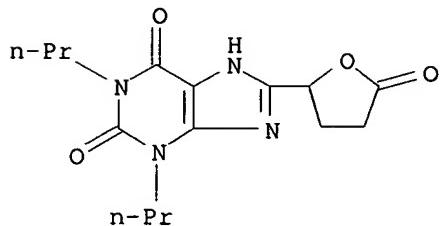
Searched by: Mary Hale 308-4258 CM-1 1E01

dipropyl-1H-purin-8-yl)-2-furanyl]propyl]- (9CI) (CA INDEX NAME)



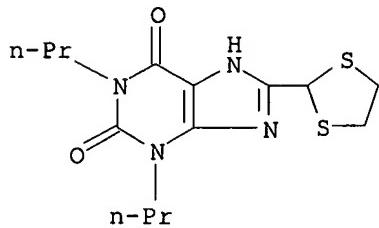
RN 133058-65-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(tetrahydro-5-oxo-2-furanyl)- (9CI) (CA INDEX NAME)



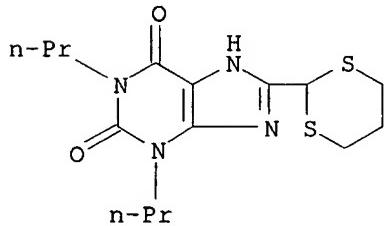
RN 133058-66-9 HCPLUS

CN 1H-Purine-2,6-dione, 8-(1,3-dithiolan-2-yl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 133058-71-6 HCPLUS

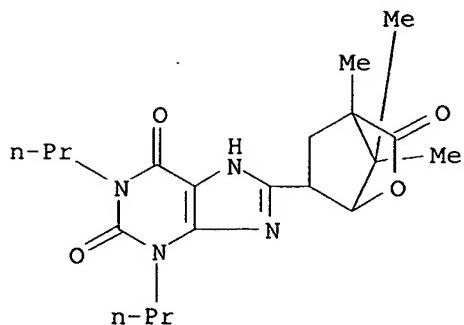
CN 1H-Purine-2,6-dione, 8-(1,3-dithian-2-yl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 133058-84-1 HCPLUS

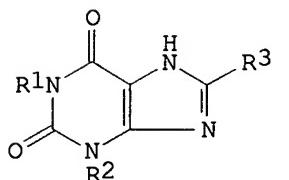
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(4,7,7-trimethyl-3-oxo-2-

oxabicyclo[2.2.1]hept-6-yl)- (9CI) (CA INDEX NAME)



L5 ANSWER 85 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
1991:102033 Document No. 114:102033 Preparation of 1,3-dialkyl-8-substituted-xanthines as drugs. Maschler, Harald; Spicer, Barbara Ann; Smith, Harry (Beecham-Wuelfing G.m.b.H. und Co. K.-G., Germany; Beecham Group PLC). Eur. Pat. Appl. EP 389282 A2 19900926, 24 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-303093 19900322. PRIORITY: GB 1989-6792 19890323.

GI



I

AB The title compds. [I; R1,R2 = alkyl, (CH<sub>2</sub>)<sub>m</sub>A; m = 1-3; A = (substituted) cyclic hydrocarbyl; R3 = halo, NO<sub>2</sub>, amino, acylamino], were prep'd. Thus, 1,3-dibutylxanthine in HOAc was treated with conc. HNO<sub>3</sub> at 87.degree. to give 86% 1,3-dibutyl-8-nitroxanthine. The latter in conc. HCl was treated with Sn to give 63% 1,3-dibutyl-8-aminoxanthine hydrochloride. The latter inhibited cAMP phosphodiesterase with Ki = 1.3 .mu.M.

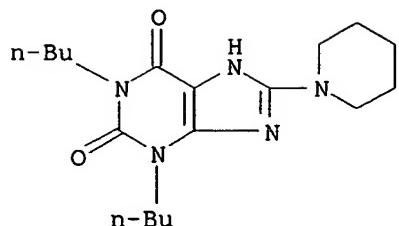
IT 132186-73-3P 132186-74-4P 132186-75-5P

132186-76-6P 132186-77-7P 132210-44-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, as drug)

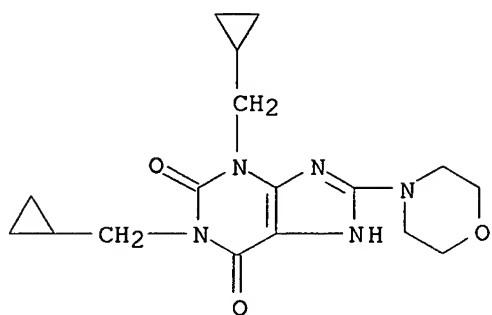
RN 132186-73-3 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



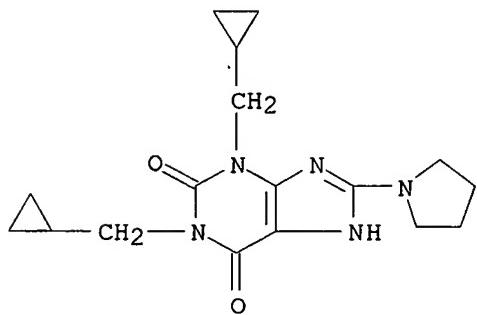
RN 132186-74-4 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(4-morpholinyl)- (9CI) (CA INDEX NAME)



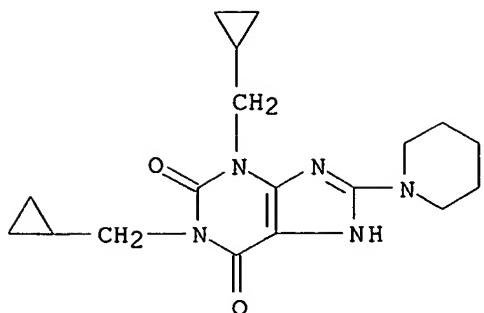
RN 132186-75-5 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



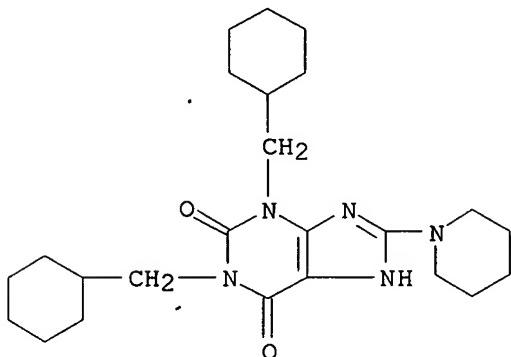
RN 132186-76-6 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-bis(cyclopropylmethyl)-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



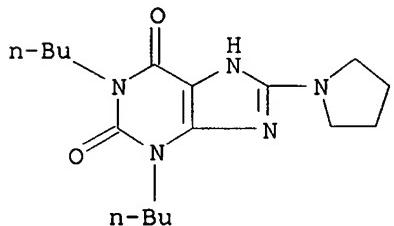
RN 132186-77-7 HCAPLUS

CN 1H-Purine-2,6-dione, 1,3-bis(cyclohexylmethyl)-3,7-dihydro-8-(1-piperidinyl)- (9CI) (CA INDEX NAME)



RN 132210-44-7 HCAPLUS

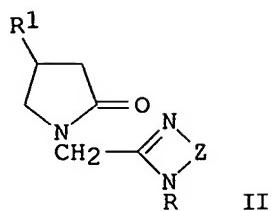
CN 1H-Purine-2,6-dione, 1,3-dibutyl-3,7-dihydro-8-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 86 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1991:101601 Document No. 114:101601 Synthesis and pharmacological properties of amidine analogs of pyracetam. Voronina, T. A.; Glotman, O. M.; Orlova, E. K.; Meshcheryakova, L. M.; Zauer, V.; Eckard, R.; Garibova, T. L.; Rakhamankulova, I. Kh.; Rostock, A.; Siegemund, H. (NII Famakol., Moscow, USSR). Khimiko-Farmatsevticheskii Zhurnal, 24(11), 26-9 (Russian) 1990. CODEN: KHFZAN. ISSN: 0023-1134. OTHER SOURCES: CASREACT 114:101601.

GI



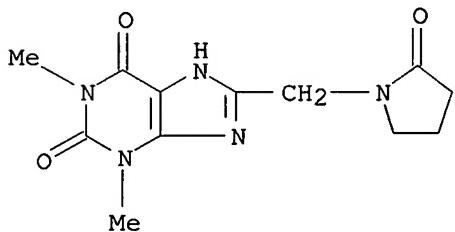
**AB** Cyclocondensation of 2-oxopyrrolidine-1-acetonitrile (I) with o-(H<sub>2</sub>N)<sub>2</sub>C<sub>6</sub>H<sub>4</sub> or 3,4-diaminopyridine in polyphosphoric acid gave 37.0-48.0% in title compds. II (R = R<sub>1</sub> = H; Z = o-C<sub>6</sub>H<sub>4</sub>, 3,4-pyridinediyl) as the oxalates. 4-Phenylpyrrolidin-2-one reacted with NaOMe in refluxing PhMe and then with ClCH<sub>2</sub>CO<sub>2</sub>Me to give 88.8% Me 2-oxo-4-phenylpyrrolidine-1-acetate (III), which cyclized at 150.degree. in the presence of NH<sub>4</sub>Cl to give 51.5% II (R = H, R<sub>1</sub> = Ph, Z = o-C<sub>6</sub>H<sub>4</sub>). Treating I with EtOH in CHCl<sub>3</sub>-Et<sub>2</sub>O contg. dry HCl and then with H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NHR<sub>2</sub> (R<sub>2</sub> = H, CH<sub>2</sub>Ph) gave 21.0-42.2% II.C<sub>2</sub>H<sub>2</sub>O<sub>4</sub> (R = R<sub>2</sub>, R<sub>1</sub> = H, Z = CH<sub>2</sub>CH<sub>2</sub>), which was acetylated with Ac<sub>2</sub>O in dioxane to give 24.2% II (R = Ac, R<sub>1</sub> = H, Z = CH<sub>2</sub>CH<sub>2</sub>). III reacted with 4,5-diamino-1,3-dimethyluracil to give 37.9% monoacetamido deriv., which underwent intramol. cyclocondensation to give 63.9% II theophylline analog. II had nootropic activities similar to pyrazetam.

**IT** 132351-23-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. and nootropic activity of)

RN 132351-23-6 HCPLUS

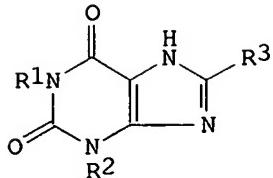
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(2-oxo-1-pyrrolidinyl)methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 87 OF 163 HCPLUS COPYRIGHT 2002 ACS

1991:61844 Document No. 114:61844 Preparation of xanthine derivatives having bronchodilating activity. Poli, Stefano; Del Corona, Lucio; Coppi, Germano (Poli Industria Chimica S.p.A., Italy). Eur. Pat. Appl. EP 386683 A2 19900912, 6 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-104229 19900305. PRIORITY: IT 1989-19730 19890310.

GI



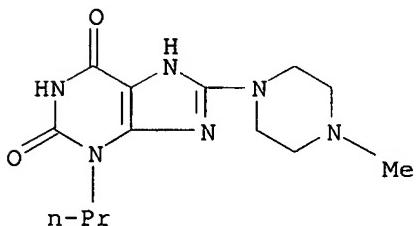
AB Title compds. I (R1 = H, C1-6 alkyl, C2-6 alkoxyalkyl, C3-6 cycloalkyl, C4-7 cycloalkylmethyl; R3 = H, C1-6 alkyl, C4-6 aliph. cycloamino residue having 1 or more N), are prep'd. 1-(Cyclopropylmethyl)-5-amino-6-formylamino)uracil (prepn. given) was suspended in 2N NaOH, heated to 90.degree. for 2 h, cooled and acidified with AcOH to give I (R1 = R3 = H; R2 = cyclopropylmethyl). Similarly prep'd. was I (R1 = H; R2 = Pr; R3 = 4-methylpiperazinyl).2HCl (II). In test for broncholating activity (bronchoconstriction induced in guinea pig by histamine), II at 10 mg/kg, i.p. showed inhibition of 97.6%.

IT 131627-57-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as bronchodilator)

RN 131627-57-1 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-methyl-1-piperazinyl)-3-propyl-  
(9CI) (CA INDEX NAME)



L5 ANSWER 88 OF 163 HCPLUS COPYRIGHT 2002 ACS

1990:584544 Document No. 113:184544 Effects of the methylxanthine S 9795 on isolated bronchi of the dog. Busk, Michael F.; Flavahan, Nicholas A.; Vanhoutte, Paul M. (Mayo Clin., Mayo Found., Rochester, MN, USA). Journal of Pharmacology and Experimental Therapeutics, 254(3), 1045-53 (English) 1990. CODEN: JPETAB. ISSN: 0022-3565.

AB The xanthine deriv. is a potent inhibitor of bronchoconstriction in vivo. The effects of S-9795 in vitro on the dog autonomic nerves and the epithelium or the smooth muscle of the bronchial wall were studied. S-9795 was more potent against contractions evoked by nerve stimulation. S-9795 caused the release of [3H]norepinephrine from the adrenergic nerve endings but did not affect neuronal uptake of the catecholamine. At low concns., S-9795 acted as a competitive serotonergic antagonist; at higher concns., the compd. inhibited noncompetitively the contractions evoked by histamine and acetylcholine. In the second and fourth order bronchi, S-9795 (and theophylline) produced concn.-dependent relaxations that were greater in rings with, compared with rings without, epithelium. The compd. also facilitated the epithelium-dependent component of the relaxation response to .beta.-adrenergic activation. S-9795 may cause prejunctional inhibition of the release of acetylcholine, evoke the displacement of stored norepinephrine, exert a differential inhibitory

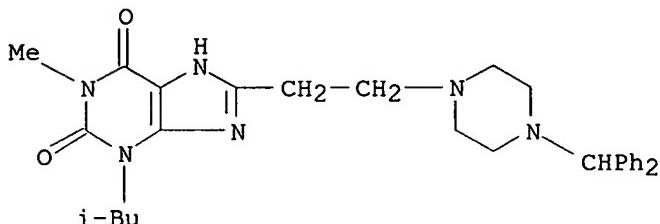
effect on airway contractions induced by various bronchoconstrictors, and augment the release or facilitates the effect of the epithelium-derived relaxing factor. These effects could contribute to the bronchodilator effect of the drug.

IT 90749-32-9, S-9795

RL: BIOL (Biological study)  
(bronchodilation from, mechanism of)

RN 90749-32-9 HCAPLUS

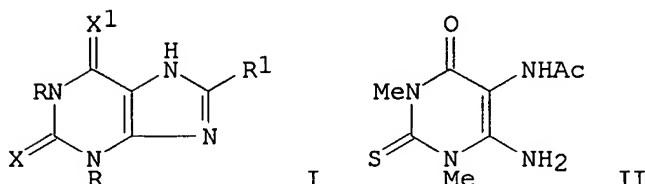
CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 89 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1990:552156 Document No. 113:152156 Sulfur-containing xanthine derivatives as adenosine antagonists. Jacobson, K. A.; Pfleiderer, W.; Daly, J. W.; Neumeyer, J. L. (National Institute of Diabetes and Digestive and Kidney Diseases, USA). U. S. Pat. Appl. US 340351 A0 19900315, 33 pp. Avail. NTIS Order No. PAT-APPL-7-340 351. (English). CODEN: XAXXAV.  
APPLICATION: US 1989-340351 19890419.

GI



AB Thioxanthine derivs. [I; R = (substituted) C1-12 alkyl; R1 = H, (substituted) furyl, thiienyl, cycloalkyl, Ph; X, X1 = O, S; X = X1 .noteq. O], useful as A1- or A2-adenosine receptor antagonists, are prep'd. Heating thiouracil II under reflux in 1N NaOH and EtOH and acidification with HOAc gave 91% thioxanthine I (R = R1 = Me, X = S, X1 = O), which showed Ki = 8 against A2-receptor binding and 1390 .+-. 88 against A2-receptor binding. Also prep'd. and tested were 18 addnl. I.

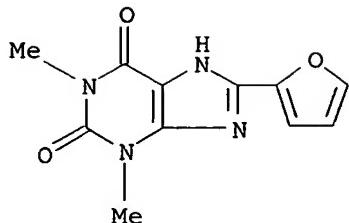
IT 33797-74-9P 33797-75-0P 93214-93-8P

117027-85-7P 121542-92-5P 121542-93-6P

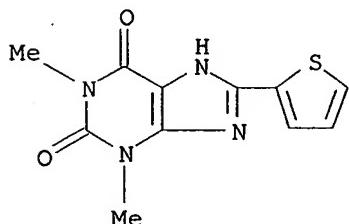
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as adenosine antagonist)

RN 33797-74-9 HCAPLUS

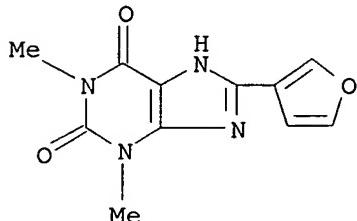
CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



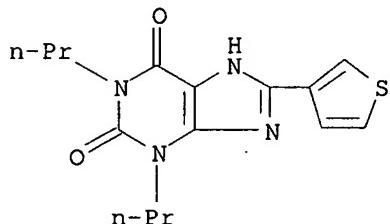
RN 33797-75-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



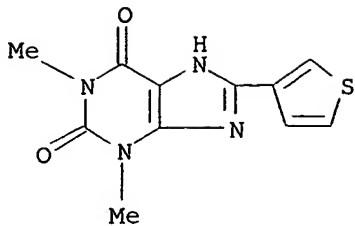
RN 93214-93-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-(3-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 117027-85-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)

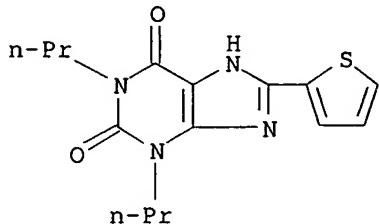


RN 121542-92-5 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



RN 121542-93-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 90 OF 163 HCPLUS COPYRIGHT 2002 ACS

1990:528988 Document No. 113:128988 Electrochemiluminescent rhenium compounds, their preparation, and analytical methods using them. Massey, Richard J.; Powell, Michael J.; Dressick, Walter J.; Leland, Jonathan K.; Hino, Janel K.; Poonian, Mohindar S.; Della, Ciana Leopoldo (IGEN Inc., USA). PCT Int. Appl. WO 8904302 A1 19890518, 160 pp. DESIGNATED STATES: W: AU, BR, DK, FI, JP, KR, NL, NO, SU; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1988-US3947 19881104. PRIORITY: US 1987-117017 19871104.

AB Electrochemiluminescent compds. ( $\text{RePmLlnL2oL3pL4qL5rL6s}$ ) $t\text{Bu}$  ( $P$  is a polydentate ligand of  $\text{Re}$ ;  $L1-L6$  are ligands of  $\text{Re}$ ;  $B$  is a ligand of  $\text{Re}$  or is conjugated to  $\text{.gtoreq.}1$  of  $P$ ,  $L1$ ,  $L2$ ,  $L3$ ,  $L4$ ,  $L5$ , or  $L6$ ;  $m$ ,  $t$ ,  $u$   $\text{.gtoreq.}1$ ;  $n$ ,  $o$ ,  $p$ ,  $q$ ,  $r$ ,  $s = 0$  or an integer) ( $I$ ) are provided;  $P$ ,  $L1$ ,  $L2$ ,  $L3$ ,  $L4$ ,  $L5$ ,  $L6$ , and  $B$  are of such compn. and no. that  $I$  can be induced to emit electromagnetic radiation and the total no. of bonds to  $\text{Re}$  provided by the ligands are equal to the coordination of  $\text{Re}$ . Electrochemiluminescent assays using  $I$  for the detection or detn. of an analyte in a multicomponent liq. comprise (1) contacting the sample with a reagent labeled with a  $\text{Re}$ -contg. electrochemiluminescent chem. moiety and capable of combining with the analyte; and (2) exposing the resulting sample to chem., electrochem., or electromagnetic energy and detecting the electromagnetic radiation emitted by the electrochemiluminescent moiety.  $I$  are easily prep'd. compared to the analogous  $\text{Ru(II)}$  complexes, the complexes of the invention permit, by choice of  $\text{.gtoreq.}1$  substituents on the ligands bound to  $\text{Re}$ , tuning of the emission wavelength for the complexes over most of the visible spectral region; the quantum efficiencies of these complexes are also superior to those of  $\text{Ru(II)}$ . Thus, fac-(bpy) $\text{Re(CO)}_3[3\text{-}(4\text{-pyridyl})\text{-propionic acid}] \text{ClO}_4\cdot\text{H}_2\text{O}$  ( $\text{II}$ ) (fac = facial isomer; bpy = 2,2'-bipyridine) was prep'd. by refluxing fac-(bpy) $\text{Re(CO)}_3\text{CF}_3\text{SO}_3$  and 3-(4-pyridyl)-propionic acid in EtOH and  $\text{H}_2\text{O}$  for 4 h in an Ar atm. After removal of the solvent,  $\text{II}$  was purified by Sephadex SP-25 chromatog. Rabbit anti-mouse IgG antibody was labeled with  $\text{II}$  and electrochemiluminescence of solns. contg. various concns. of the

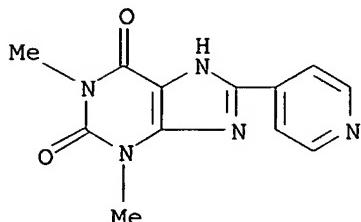
conjugate were measured (app. described). The sensitivity of the assay for the labeled antibody was 1 .times. 10<sup>-9</sup>M. Use of the compds. of the invention in immunoassays for theophylline detn. and as DNA hybridization probes are described.

IT 1088-64-8P 129052-70-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of, for electrochemiluminescence reagent)

RN 1088-64-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



RN 129052-70-6 HCPLUS

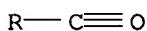
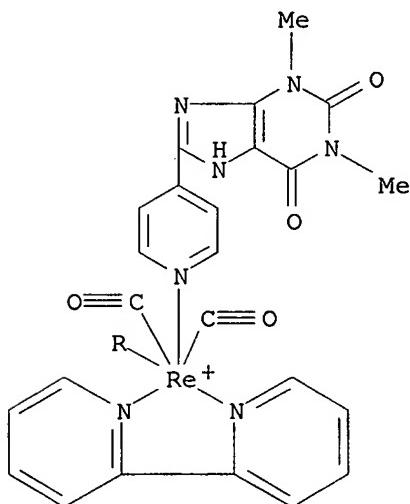
CN Rhenium(1+), (2,2'-bipyridine-N,N')tricarbonyl[3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)-1H-purine-2,6-dione-N8]-, (OC-6-33)-, salt with trifluoromethanesulfonic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 129052-69-3

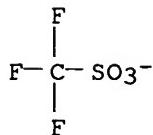
CMF C25 H19 N7 O5 Re

CCI CCS

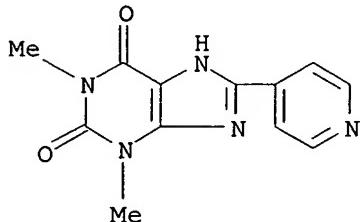


CM 2

CRN 37181-39-8  
CMF C F3 O3 S

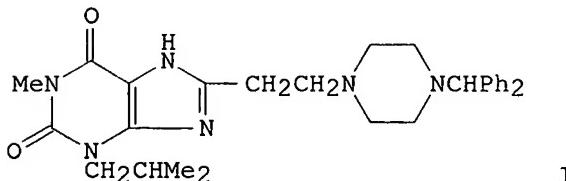


IT 1088-64-8, 8-(4-Pyridyl)-theophylline  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, in rhenium complex prepn. for electrochemiluminescence anal.)  
RN 1088-64-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 91 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
1990:491249 Document No. 113:91249 Effect of a new xanthine derivative on the release of insulin from rat pancreatic islets. Devreux, V.; Plasman, P. O.; Lebrun, P.; Herchuelz, A. (Sch.Med., Brussels Univ., Brussels, Belg.). Arzneimittel-Forschung, 40(3), 268-71 (English) 1990. CODEN: ARZNAD. ISSN: 0004-4172.

GI



I

AB S 9795 (I) is a new xanthine deriv. displaying antiasthmatic properties in animals. I might exert its pharmacol. actions either by inhibiting phosphodiesterases, or by inhibiting cellular Ca<sup>2+</sup> movements or antagonizing purinoreceptors. Since the process of glucose-induced insulin release is markedly influenced by xanthine derivs., the effect of I was compared to 2 other xanthine derivs. [theophylline and 3-isobutyl-1-methylxanthine (IBMX)] on glucose-induced insulin release and ionic fluxes in rat pancreatic islets. Theophylline and IBMX potentiated glucose-induced insulin release, while I inhibited the insulinotropic effect of glucose. The effect of I was obsd. at 10<sup>-5</sup> mol/L, lower concns.

(10<sup>-6</sup> to 10<sup>-9</sup> mol/L) failing to affect glucose-induced insulin release. At 10<sup>-5</sup> mol/L, I also inhibited the secondary rise in 45Ca efflux evoked by glucose from preloaded islets and the uptake of 45Ca by incubated islets stimulated either by glucose or K. I failed to alter 86Rb fluxes in stimulated and unstimulated islets labeled with the radioisotope. These data show that I inhibits glucose-induced insulin release, possibly by blocking glucose-stimulated Ca<sup>2+</sup> inflow into the B-cell.

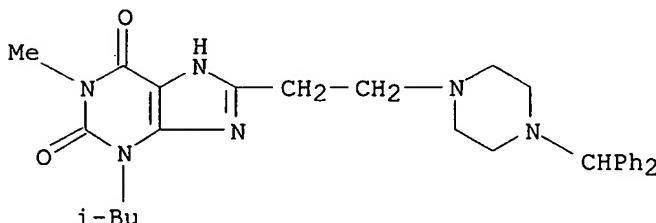
IT 90749-32-9, S 9795

RL: BIOL (Biological study)

(insulin release from pancreatic islets, inhibition by, as xanthine deriv., inhibition of calcium uptake in)

RN 90749-32-9 HCAPLUS

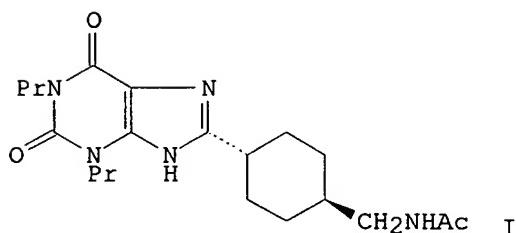
CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 92 OF 163 HCAPLUS COPYRIGHT 2002 ACS

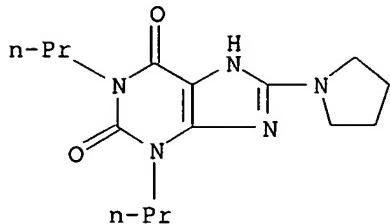
1990:478009 Document No. 113:78009 Structure-activity relationships of 8-cycloalkyl-1,3-dipropylxanthines as antagonists of adenosine receptors. Katsushima, T.; Nieves, L.; Wells, J. N. (Sch. Med., Vanderbilt Univ., Nashville, TN, 37232, USA). Journal of Medicinal Chemistry, 33(7), 1906-10 (English) 1990. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 113:78009.

GI



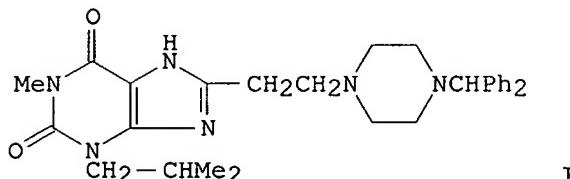
AB A series of 8-substituted 1,3-dipropylxanthines was prep'd. and their potency as antagonists of A1 and A2 adenosine receptors of human platelets and rat adipocytes, resp., were detd. No agents studied were as potent as 8-cyclopentyl-1,3-dipropylxanthine as antagonists of the A1 adenosine receptor, but 8-(2-methylcyclopropyl)-1,3-dipropylxanthine was at least 1000-fold more potent as an antagonist of A1 than of A2 adenosine receptors. While most substitutions on the 8-cycloalkyl moiety caused decreased inhibition of both A1 and A2 adenosine receptors, the acetamidomethylcyclohexylxanthine I was nearly equipotent as an antagonist of the two receptors and appeared to be the most potent antagonist of A2

adenosine receptors reported to date.  
 IT 127946-21-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. and adenosine receptor antagonist activity of)  
 RN 127946-21-8 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(1-pyrrolidinyl)- (9CI)  
 (CA INDEX NAME)



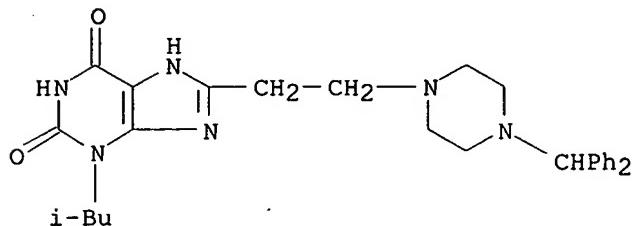
L5 ANSWER 93 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
 1990:131828 Document No. 112:131828 Kinetics and brain uptake of S 9795, a new xanthine derivative, in rats. Bianchi, G.; Caccia, S.; Della Vedova, F.; Garattini, S. (Ist. Ric. Farmacol. "Mario Negri", Milan, Italy). European Journal of Drug Metabolism and Pharmacokinetics, 14(3), 201-8 (English) 1989. CODEN: EJDPD2. ISSN: 0398-7639.

GI

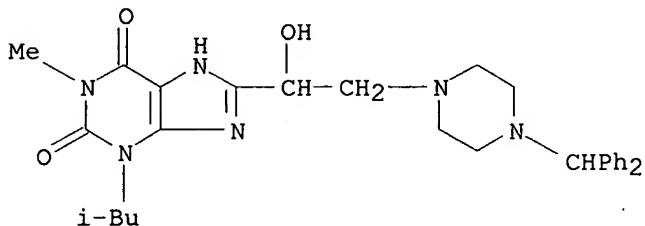


AB The relationships between plasma and brain concns. of S 9795 (I) and its main metabolites after single i.v. doses of S 9795 were examd. in rats by HPLC with UV detection. S 9795 disappeared from plasma and brain almost in parallel, with comparable elimination half-lives of .apprx.0.8 h, regardless of the dose. The vol. of distribution was high (.apprx.3 L/kg), but total clearance was also high (.apprx.40 mL/min/kg) and this explains the relatively short plasma and brain half-lives of the drug in the rat. Among the possible metabolites examd., the N-dearylated metabolite S 10238 rapidly appeared in both plasma and brain. Thereafter, S 10238 was likewise eliminated in parallel from both compartments, although at a slower rate (half-life .apprx.1.4 h) than its parent compd. Norcyclizine, a metabolite resulting from cleavage of the parent drug side-chain, was detected only in the brain and only at the highest dose tested. The plasma/brain ratio of the area under the concn.-time curves was slightly <1 for S 9795, .apprx.0.1 for S 10238 and possibly >2 for norcyclizine, this latter being present in rat plasma at concns. below the limits of sensitivity of the method (0.08 nmol/mL). The results indicate that S 9795 and some of its metabolites enter the central nervous system, although to different extents, and support the hypothesis that the lack of central effects of S 9795 is probably the consequence of the poor brain adenosine receptor antagonism by this compd.

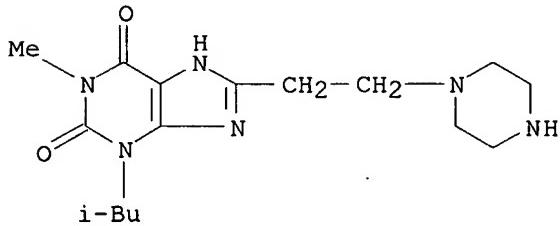
IT 110480-48-3, S 10257 110480-52-9, S 10337  
 121661-38-9, S 10238  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (pharmacokinetics of, as S 9795 metabolite, in brain and blood)  
 RN 110480-48-3 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-  
 dihydro-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



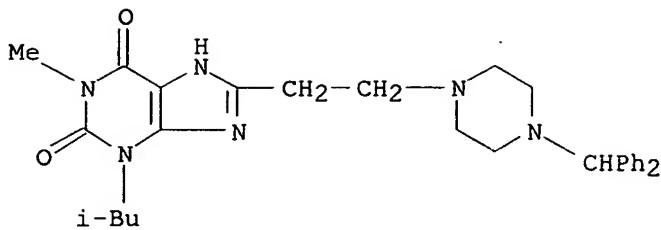
RN 110480-52-9 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]-1-  
 hydroxyethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX  
 NAME)



RN 121661-38-9 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-(2-methylpropyl)-8-[2-(1-  
 piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



IT 90749-32-9, S 9795  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (pharmacokinetics of, in brain and blood)  
 RN 90749-32-9 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-  
 dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

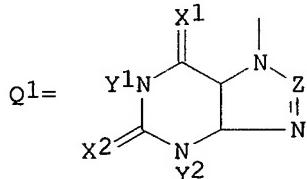
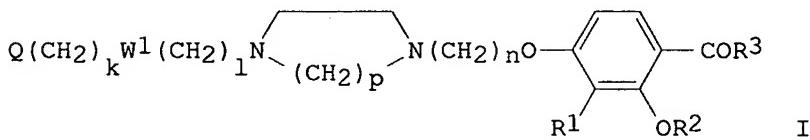


L5 ANSWER 94 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1990:35563 Document No. 112:35563 Preparation of xanthine derivatives as leukotriene antagonists. Suzuki, Fumio; Shimada, Junichi; Hayashi, Hiroaki; Oomori, Takemori; Manabe, Haruhiko (Kyowa Hakko Kogyo Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 01156978 A2 19890620 Heisei, 22 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1988-169572 19880707.

PRIORITY: JP 1987-239270 19870924.

GI

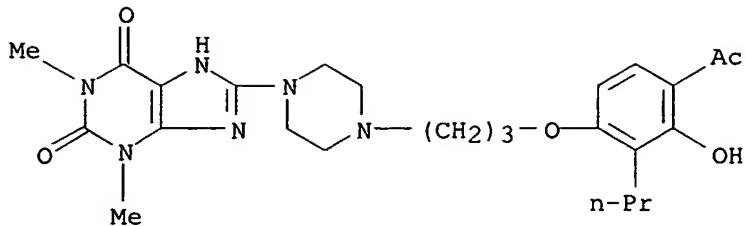


AB The title compds. I [Q = xanthine, 8-azaxanthine residue (e.g., Q1, etc.); Z = N, CY3; Y1-Y3 = H, alkyl, alkenyl, etc.; X1, X2 = O, S; W1, W2, CH2, CHO, etc.; A = H, acyl; R1 = alkyl, alkenyl; R2 = H, acyl; R3 = H, alkyl, cycloalkyl; k, l, m, n = 0-4; p = 1-3] and salts thereof, useful as leukotriene antagonists, were prepd. A mixt. of 1,3-dimethyl-7-(3-iodopropyl)xanthine, 2-hydroxy-3-propyl-4-[3-(1-piperazinyl)propoxy]acetophenone, and Et3N in EtOH was refluxed for 2.5 h to give, after acidification with HCl, 69% 7-[3-[4-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propyl]1-piperazinyl]propyl]-1,3-dimethylxanthine-3HCl (II). II exhibited an IC50 of 0.93 .mu.M against leukotriene D4 in a test using guinea pig tracheal strips.

IT 124459-26-3P 124481-20-5P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepns. of, as leukotriene antagonist)

RN 124459-26-3 HCAPLUS

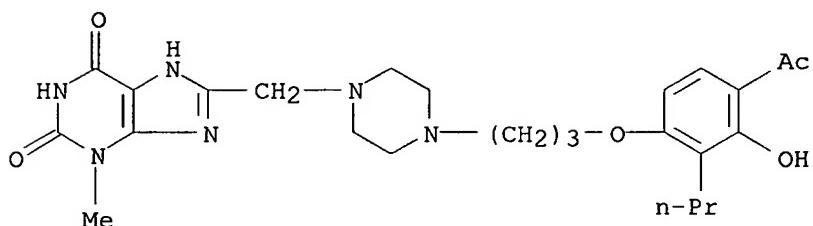
CN 1H-Purine-2,6-dione, 8-[4-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propyl]-1-piperazinyl]-3,7-dihydro-1,3-dimethyl-, hydrochloride (2:3) (9CI) (CA INDEX NAME)



● 3/2 HCl

RN 124481-20-5 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[(4-acetyl-3-hydroxy-2-propylphenoxy)propyl]-1-piperazinylmethyl-3,7-dihydro-3-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

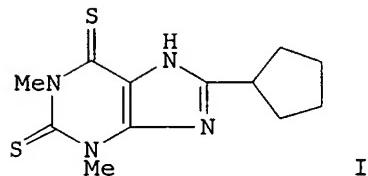


● HCl

L5 ANSWER 95 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1989:477745 Document No. 111:77745 Sulfur-containing 1,3-dialkylxanthine derivatives as selective antagonists at A<sub>1</sub>-adenosine receptors. Jacobson, Kenneth A.; Kiriasis, Leonidas; Barone, Suzanne; Bradbury, Barton J.; Kammula, Udai; Campagne, Jean Michel; Daly, John W.; Neumeyer, John L.; Pfleiderer, Wolfgang; Secunda, Sherrie (Lab. Chem. Bioorg. Chem., NIDDK, Bethesda, MD, 20892, USA). Journal of Medicinal Chemistry, 32(8), 1873-9 (English) 1989. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 111:77745.

GI



AB Sulfur-contg. analogs, e.g. I, of 8-substituted xanthines were prepd. in an effort to increase selectivity or potency as antagonists at adenosine receptors. Either cyclopentyl or various aryl substituents were utilized

at the 8-position, because of the assocn. of these groups with high potency at A1-adenosine receptors. Sulfur was incorporated on the purine ring at positions 2 and/or 6, in the 8-position substituent in the form of 2- or 3-thienyl groups, or via thienyl groups sepd. from an 8-aryl substituent through an amide-contg. chain. The feasibility of using the thienyl group as a prosthetic group for selective iodination via its Hg<sup>2+</sup> deriv. was explored. Receptor selectivity was detd. in binding assays using membrane homogenates from rat cortex or striatum for A1- and A2-adenosine receptors, resp. Generally, 2-thio-8-cycloalkylxanthines were at least as A1 selective as the corresponding oxygen analog. 2-Thio-8-aryl derivs. tended to be more potent at A2 receptors than the oxygen analog. 1,3-Dipropyl-8-(2-thienyl)-2-thioxanthine was >285-fold as A1 selective.

IT 33797-75-0P 117027-85-7P 121542-92-5P

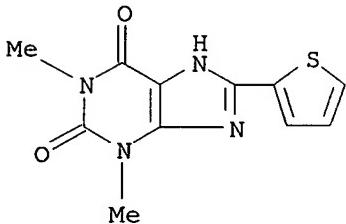
121542-93-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and A1-adenosine receptor antagonist activity of)

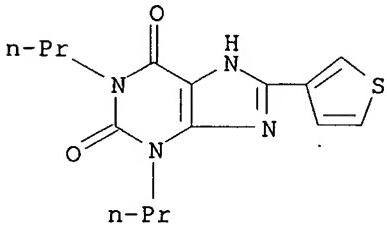
RN 33797-75-0 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



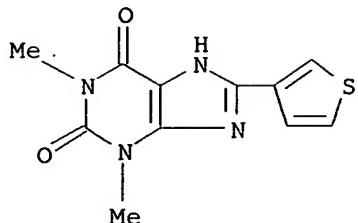
RN 117027-85-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



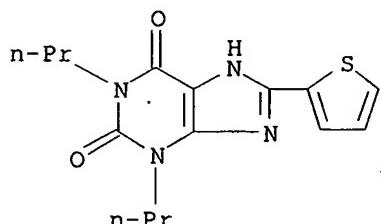
RN 121542-92-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



RN 121542-93-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 96 OF 163 HCPLUS COPYRIGHT 2002 ACS

1989:470719 Document No. 111:70719 Effects of theophylline and S 9795 on hyperoxic and hypoxic pulmonary vascular tone in intact dogs. Lejeune, P.; Leeman, M.; Melot, C.; Naeije, R. (Dep. Intensive Care, Erasme Univ. Hosp., Brussels, 1070, Belg.). European Respiratory Journal, 2(4), 370-6 (English) 1989. CODEN: ERJOEI. ISSN: 0903-1936.

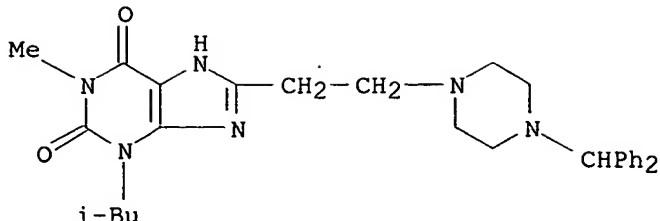
AB The effects of theophylline and of S 9795, a new methylxanthine deriv., on multipoint mean pulmonary arterial pressure (Ppa)/cardiac index (.ovrhdot.Q) relationships were studied in intact dogs ventilated alternately in hyperoxia (fraction of inspired oxygen, FIO<sub>2</sub> 0.4) and in hypoxia (FIO<sub>2</sub> 0.1). A sequence of two 5-point Ppa/.ovrhdot.Q plots at FIO<sub>2</sub> 0.4 and 0.1 was performed before and after i.v. administrations of theophylline (10 and 25 mg/kg) or S 9795 (10 mg/kg). The Ppa/.ovrhdot.Q plots were rectilinear in all exptl. conditions. Over the entire range of .ovrhdot.Q studied, 2-5 L.cntdot.min-1.cntdot.m-2, hypoxia increased Ppa in all animals. Placebo had no effect on the Ppa/.ovrhdot.Q plots. Theophylline at the lowest dose (plasma levels 8.4-13.6 .mu.g/mL) and S 9795 (plasma levels 3.0-11.2 .mu.g/mL) did not affect Ppa/.ovrhdot.Q in hyperoxia or in hypoxia. Theophylline at the highest dose (plasma levels 17.8-40.4 .mu.g/mL) reduced hypoxic Ppa at all levels of .ovrhdot.Q and hyperoxic Ppa at the highest .ovrhdot.Q, from 3-5 L.cntdot.min-1.cntdot.m-2, and inhibited hypoxia-induced increases in Ppa. Pulmonary vasoconstriction may be preserved after the lowest doses of methylxanthines recommended for the treatment of increased bronchial tone.

IT 90749-32-9, S-9795

RL: BIOL (Biological study)  
(lung vessel tone response to, in hypoxia and hyperoxia)

RN 90749-32-9 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 97 OF 163 HCPLUS COPYRIGHT 2002 ACS

1989:449907 Document No. 111:49907 8-Substituted xanthines as phosphodiesterase inhibitors: conformation-dependent lipophilicity and structure-activity relationships. Walther, Bernard; Carrupt, Pierre Alain; El Tayar, Nabil; Testa, Bernard (Ec. Pharm., Univ. Lausanne, Lausanne, CH-1005, Switz.). Helvetica Chimica Acta, 72(3), 507-17 (English) 1989. CODEN: HCACAV. ISSN: 0018-019X.

AB Twenty-one 8-substituted xanthines, caffeine, and 3 isomeric dimethylxanthines were examd. for their lipophilic behavior by reversed-phase HPLC. A no. of flexible compds. showed a smaller-than-expected lipophilicity, which, based on conformational and tautomeric calcns., was ascribed to the predominance of folded forms. A QSAR anal. of the phosphodiester-inhibitory potency of several compds. showed favorable factors to be a low lipophilicity and the absence of a substituent on the N7 position.

IT 90749-32-9 90749-33-0 90749-42-1

90749-57-8 90773-95-8 110480-48-3

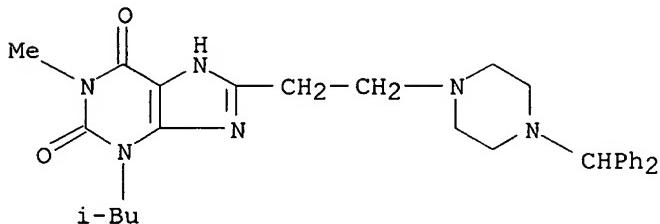
121661-37-8 121661-38-9 121678-85-1

RL: BIOL (Biological study)

(phosphodiester inhibition by and lipophilicity of, QSAR of)

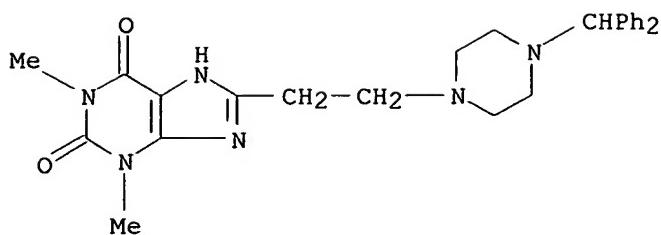
RN 90749-32-9 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



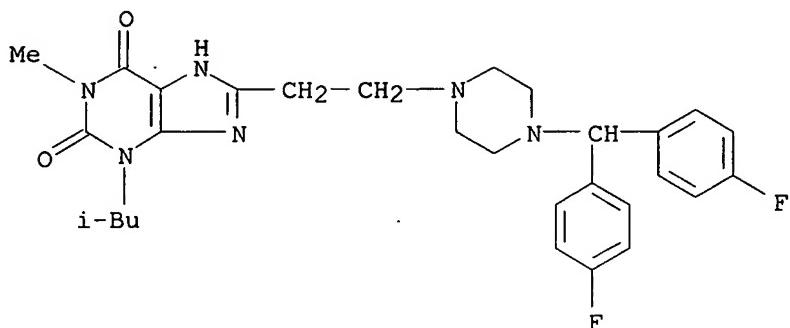
RN 90749-33-0 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



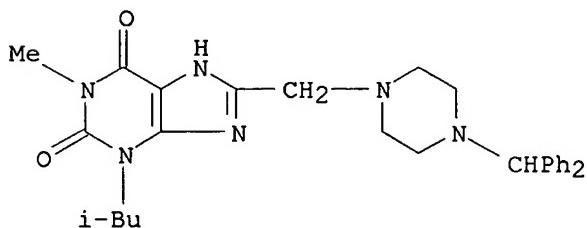
RN 90749-42-1 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-[bis(4-fluorophenyl)methyl]-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



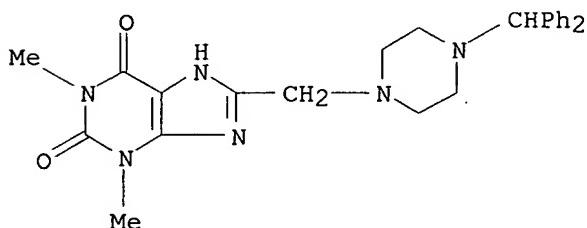
RN 90749-57-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[4-(diphenylmethyl)-1-piperazinylmethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



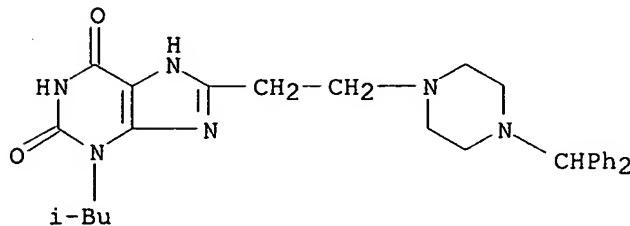
RN 90773-95-8 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[4-(diphenylmethyl)-1-piperazinylmethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



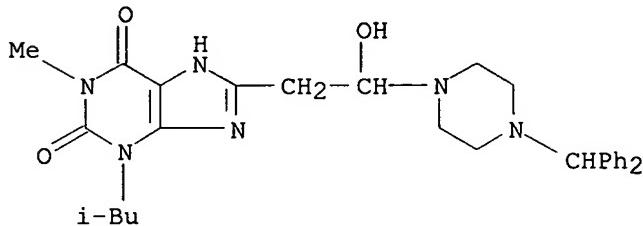
RN 110480-48-3 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-{4-(diphenylmethyl)-1-piperazinyl}ethyl]-3,7-dihydro-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



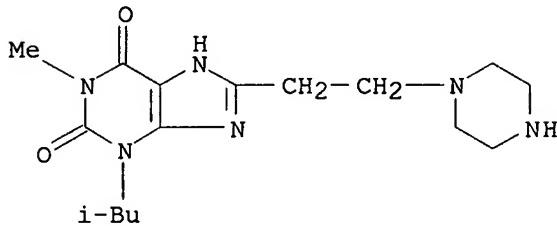
RN 121661-37-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-{4-(diphenylmethyl)-1-piperazinyl}-2-hydroxyethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



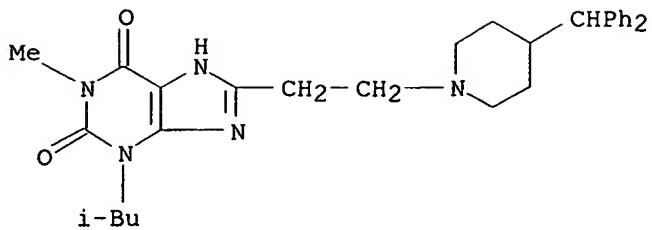
RN 121661-38-9 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-(2-methylpropyl)-8-[2-(1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 121678-85-1 HCPLUS

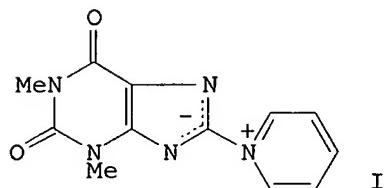
CN 1H-Purine-2,6-dione, 8-[2-{4-(diphenylmethyl)-1-piperidinyl}ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 98 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1989:423275 Document No. 111:23275 Substitution of bromine by pyridine in 8-bromotheophylline in the presence of o-phenylene phosphoric acid isocyanate. Bobkov, V. N.; Zvolinskaya, T. V.; Kuz'menko, I. I. (Kiev. Gos. Univ., Kiev, 252017, USSR). Khimiya Geterotsiklicheskikh Soedinenii (7), 1000 (Russian) 1988. CODEN: KGSSAQ. ISSN: 0453-8234. OTHER SOURCES: CASREACT 111:23275.

GI



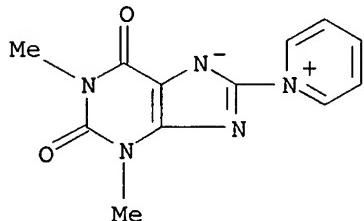
AB Heating 8-bromotheophylline in C5H5N contg. o-phenylene phosphoroisocyanatidate 2h at 100.degree. gave 77% 8-pyridiniotheophyllinate (I); when AlCl3 was the catalyst 81% I was obtained.

IT 52943-89-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 52943-89-2 HCAPLUS

CN Pyridinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



L5 ANSWER 99 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1989:224991 Document No. 110:224991 Lipophilicity and conformational behavior of substituted xanthines. Walther, B.; Carrupt, P. A.; Van de

Waterbeemd, H.; El Tayar, N.; Testa, B. (Sch. Pharm., Univ. Lausanne, Lausanne, CH-1005, Switz.). Progress in Clinical and Biological Research, 291 (QSAR: Quant. Struct.-Act. Relat. Drug Des.), 67-70 (English) 1989.  
CODEN: PCBRD2. ISSN: 0361-7742.

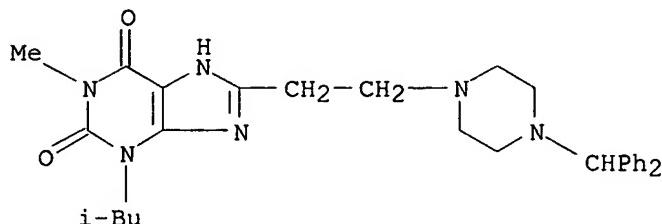
AB The lipophilicity and the conformational behavior of 18 derivs. of xanthine were investigated.

IT 90749-32-9 90749-33-0 90749-42-1  
90749-57-8 90773-95-8 110480-48-3  
110480-52-9

RL: PROC (Process)  
(lipophilicity and conformational behavior of)

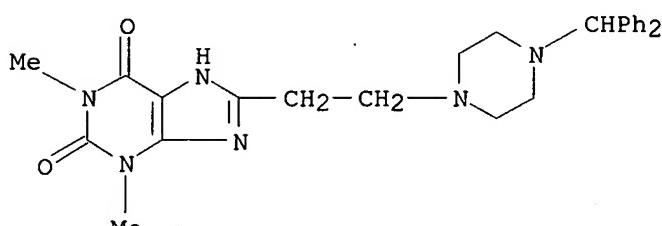
RN 90749-32-9 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



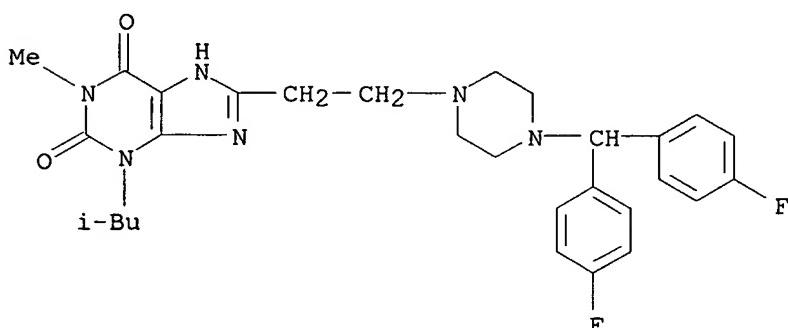
RN 90749-33-0 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

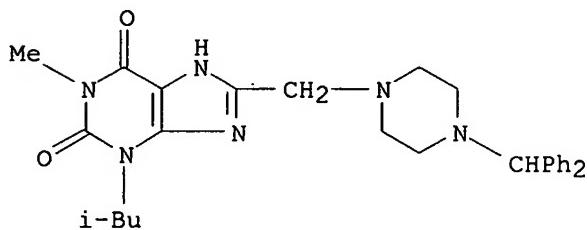


RN 90749-42-1 HCPLUS

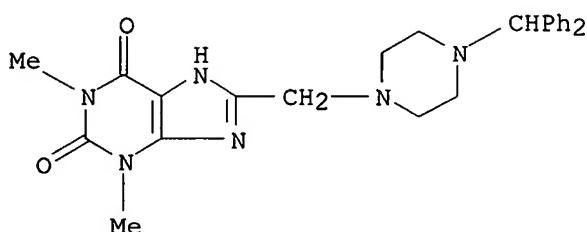
CN 1H-Purine-2,6-dione, 8-[2-[4-[bis(4-fluorophenyl)methyl]-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



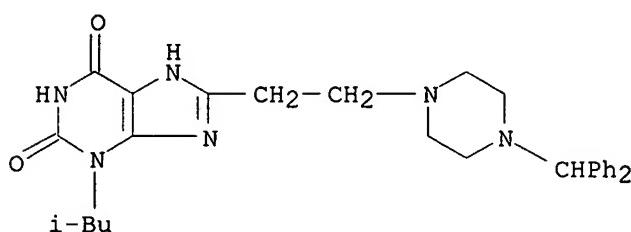
RN 90749-57-8 HCPLUS  
CN 1H-Purine-2,6-dione, 8-[[4-(diphenylmethyl)-1-piperazinyl]methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



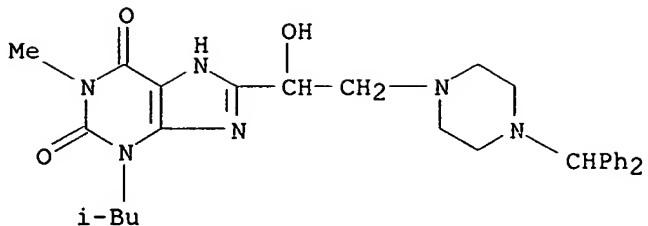
RN 90773-95-8 HCPLUS  
CN 1H-Purine-2,6-dione, 8-[[4-(diphenylmethyl)-1-piperazinyl]methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 110480-48-3 HCPLUS  
CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 110480-52-9 HCPLUS  
CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]-1-hydroxyethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 100 OF 163 HCPLUS COPYRIGHT 2002 ACS

1988:604696 Document No. 109:204696 Effects of progressively increased doses of theophylline and of S 9795 on hemodynamics, blood gases and lung mechanics in dogs. Lejeune, P.; Naeije, R. (Lab. Cardiovasc. Respir. Physiol., Erasmus Univ. Hosp., Brussels, B-1070, Belg.). Archives Internationales de Pharmacodynamie et de Therapie, 294, 215-27 (English) 1988. CODEN: AIPTAK. ISSN: 0003-9780.

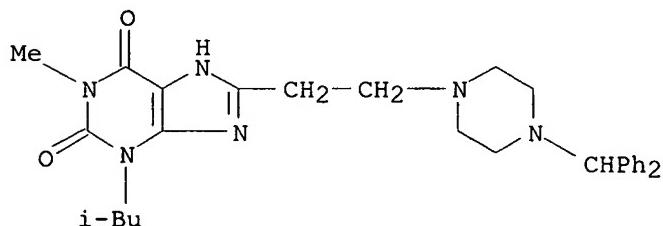
AB The effects of progressively increasing i.v. doses of theophylline and of S 9795 [1-methyl-3-isobutyl-8-(4-benzhydrylpiperazino-2-ethyl)xanthine] were studied on hemodynamics, blood gases, and lung mechanics in anesthetized dogs. The max. plasma levels that were attained were 56.6 .mu.g/mL for theophylline and 12 .mu.g/mL for S 9795. Theophylline increased heart rate and cardiac output, decreased arterial PO<sub>2</sub>, increased O consumption, and did not affect lung mechanics. S 9795 decreased heart rate, increased systemic arterial pressure, O consumption (slightly), and pulmonary capillary wedge pressure (the latter only at the highest dose), and decreased lung compliance without change in lung resistance. The effects on heart rate, O consumption, and pulmonary capillary wedge pressure differed between theophylline and S 9795. Thus, in dogs, theophylline acts as a pos. chronotropic agent, while S 9795 either has no such effect or acts as a neg. chronotropic drug at high doses. Neither of the methylxanthines appears to reduce normal bronchomotor tone.

IT 90749-32-9

RL: BIOL (Biological study)  
(blood gases and cardiovascular system and lung function response to)

RN 90749-32-9 HCPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 101 OF 163 HCPLUS COPYRIGHT 2002 ACS

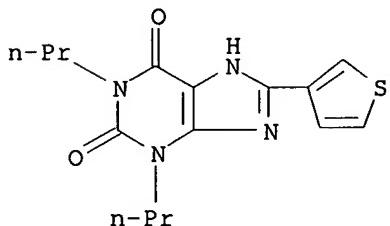
1988:590137 Document No. 109:190137 Preparation of xanthine derivatives for cognition activation. Bruns, Robert F.; Hamilton, Harriet W. (Warner-Lambert Co., USA). U.S. US 4755517 A 19880705, 7 pp. (English). CODEN: USXXAM., APPLICATION: US 1986-892538 19860731.

GI For diagram(s), see printed CA Issue.

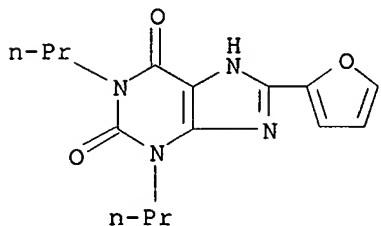
AB Title compds. I (R1, R3 = H, alkyl, hydroxyalkyl, alkoxyalkyl; R2 =

dihydroxyalkyl, Q; X = O, S, NH, C2-6 alkylimino, acylimino; m, n = 1-5) were prepd. 3-Thiophenecarboxylic acid is added to 5,6-diamino-1,3-dipropyluracil, the pH adjusted to 5, then ethyl-3-(3-dimethylamino)propylcarbodiimide is added to give 1,3-dipropyl-8-(3-thienyl)xanthine, to which in THF is added Pd/Al<sub>2</sub>O<sub>3</sub> and the mixt. reduced under a H atm of 1000 lb at 200.degree. overnight to give I (R<sub>1</sub>, R<sub>3</sub> = Me; R<sub>2</sub> = 3-tetrahydrothienyl) (II). In tests for A<sub>1</sub> receptor binding affinity (rat brain membrane) providing activity as bronchodilators, CNS stimulants, and(or) cognition activators I have an IC<sub>50</sub> value of 2 nM comparable to theophylline.

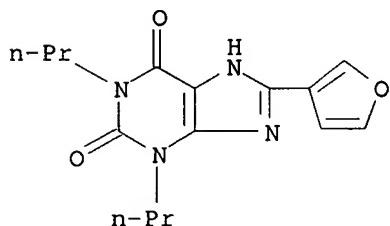
IT 117027-85-7P 117027-86-8P 117027-87-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prep. and hydrogenation of)  
 RN 117027-85-7 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(3-thienyl)- (9CI) (CA INDEX NAME)



RN 117027-86-8 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RN 117027-87-9 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-(3-furanyl)-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



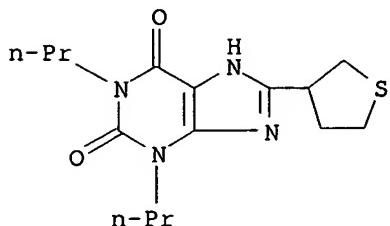
IT 117027-79-9P 117027-80-2P 117027-81-3P

**117027-82-4P 117027-83-5P 117027-84-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of, as cognition activator)

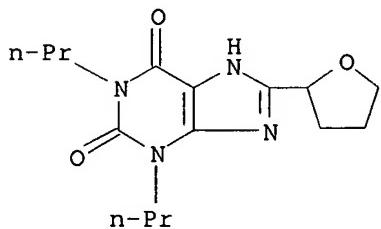
RN 117027-79-9 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(tetrahydro-3-thienyl)-  
(9CI) (CA INDEX NAME)



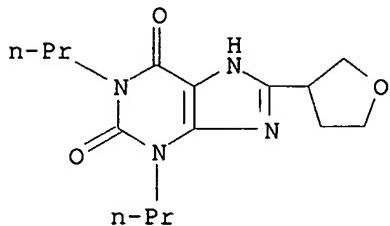
RN 117027-80-2 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(tetrahydro-2-furanyl)-  
(9CI) (CA INDEX NAME)



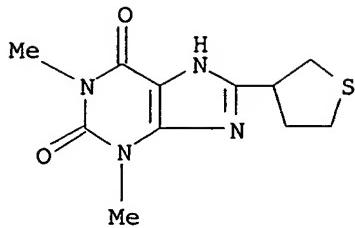
RN 117027-81-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-(tetrahydro-3-furanyl)-  
(9CI) (CA INDEX NAME)



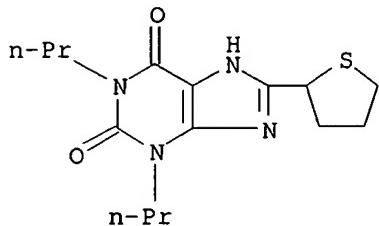
RN 117027-82-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-3-thienyl)-  
(9CI) (CA INDEX NAME)



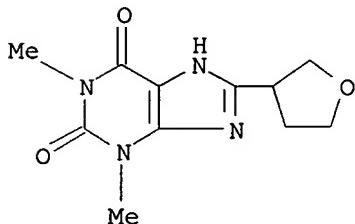
RN 117027-83-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-2-(tetrahydro-2-thienyl)-  
(9CI) (CA INDEX NAME)



RN 117027-84-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-3-furanyl)-  
(9CI) (CA INDEX NAME)



L5 ANSWER 102 OF 163 HCPLUS COPYRIGHT 2002 ACS

1988:455139 Document No. 109:55139 The crystal structure of the C-nucleoside, 1,3-dimethyl-8-.beta.-D-ribofuranosylxanthine monohydrate. Maluszynska, Hanna; Jeffrey, George A. (Dep. Crystallogr., Univ. Pittsburgh, Pittsburgh, PA, 15260, USA). Carbohydrate Research, 169, 35-42 (English) 1987. CODEN: CRBRAT. ISSN: 0008-6215.

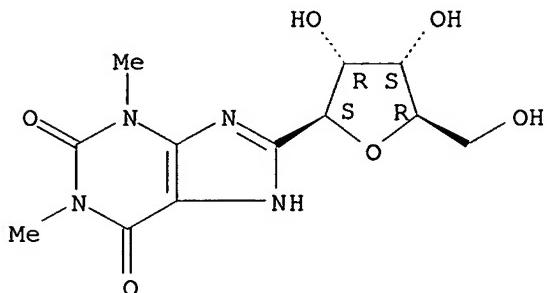
AB The crystal structure of 1,3-dimethyl-8-.beta.-D-ribofuranosylxanthine monohydrate, is reported. The ribose ring has the C-(2')-exo-C-(3')-endo (2T3) conformation and a gauche-gauche conformation around the ribose C-(4')-C-(5') bond. The .beta.-link conformation is anti. The pyrimidine and imidazole rings are planar, making an interplanar angle of 1.01(1).degree.. The mol. conformation is stabilized by an unsym., three-center H bond from N-(7)-H to O-(5')-H as the major component and to O-(4')-H as the minor component. The H bonding includes a cooperative cycle involving the HN-C-C=O moiety, two OH groups, and a water mol.

IT 115334-79-7

RL: PRP (Properties)  
(crystal and mol. structure of)

RN 115334-79-7 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-.beta.-D-ribofuranosyl-,  
monohydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● H<sub>2</sub>O

L5 ANSWER 103 OF 163 HCPLUS COPYRIGHT 2002 ACS  
1988:94512 Document No. 108:94512 8-Aryl- and 8-cycloalkyl-1,3-dipropylxanthines: further potent and selective antagonists for A1-adenosine receptors. Shamim, M. T.; Ukena, D.; Padgett, W. L.; Hong, O.; Daly, J. W. (Lab. Bioorg. Chem., Natl. Inst. Diabetes, Dig. Kidney Dis., Bethesda, MD, 20892, USA). Journal of Medicinal Chemistry, 31(3), 613-17 (English) 1988. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 108:94512.

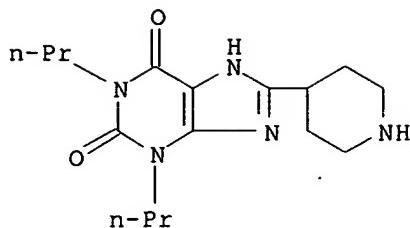
AB A series of 1,3-dipropylxanthines were prep'd. with a variety of substituents, including aryl and cycloalkyl groups, at the 8-position. Polar carboxylate and carboxamide moieties were introduced as aryl substituents to increase H<sub>2</sub>O solv. 1,3-Dipropyl-8-[2-hydroxy-4-[(carboxymethyl)oxy]phenyl]xanthine (I) is a functionalized congener with high potency (Ki = 37 nM) and selectivity (54-fold) for A1-adenosine receptors. I was used to prep. a series of other analogs, some with higher potency and some with higher selectivity. 8-Cyclopentyl- and 8-cyclohexyl-1,3-dipropylxanthines were both very potent (Ki = 1-1.5 nM) and selective for A1 receptors, while 8-cycloalkylmethyl analogs were 10-fold less potent, but still very selective for A1 receptors. 8-Piperidinyl and 8-pyrazinyl analogs had very low activities as adenosine receptor antagonists.

IT 108653-59-4P 112683-71-3P

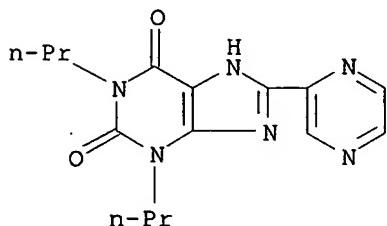
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and adenosine receptor antagonist activity of)

RN 108653-59-4 HCPLUS

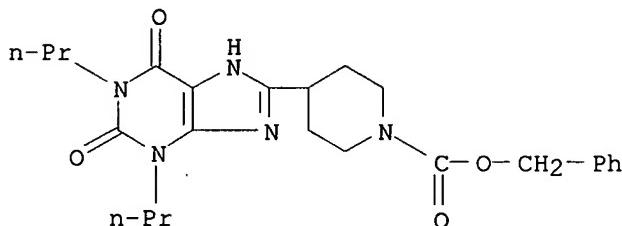
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



RN 112683-71-3 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dipropyl-8-pyrazinyl- (9CI) (CA INDEX NAME)



IT 112683-80-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prep. and deprotection of)  
 RN 112683-80-4 HCPLUS  
 CN 1-Piperidinecarboxylic acid, 4-(2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl)-, phenylmethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 104 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1988:68520 Document No. 108:68520 Pharmacological properties of a new antiasthmatic xanthine derivative devoid of central stimulatory activity. Dehault, J.; Boulanger, M.; Lonchampt, M.; Tisserand, F.; Holstorp, S.; Saint-Romas, G.; Pennel, L.; Regnier, G. (Inst. Rech. Servier, Suresnes, F-92150, Fr.). Arzneimittel-Forschung, 37(12), 1353-62 (English) 1987. CODEN: ARZNAD. ISSN: 0004-4172.

AB The bronchodilating effect and other related pharmacol. properties of an 8-amino alkyl substituted xanthine (S 9795) were compared with those of ref. drugs, in particular theophylline. The in vitro studies using the tracheal ring, taenia coli, rat peritoneal mastocytes, and enzymic preps. demonstrated the potency of S 9795 as an antiasthmatic drug, possessing protective activity superior to that of theophylline and enprofylline. S 9795 was 100-fold more active as a cAMP phosphodiesterase inhibitor than

theophylline. The compd. also protected against mast cell degranulation and consequent release of spasmogen due to antigen-antibody reaction or induced by Ca<sup>2+</sup> movements. Given orally or i.v., S 9795 had a highly selective protective effect against bronchoconstriction induced by pharmacol. reagents or allergic reactions with no demonstrable effect on the central nervous or cardiovascular systems. The pharmacol. effects of S 9795 were of longer duration than those of theophylline and enprofylline. These studies demonstrate the potential therapeutic value of S 9795 in the therapy of bronchospastic disorders.

IT 112666-96-3

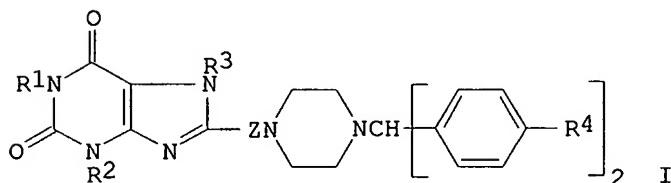
RL: BIOL (Biological study)  
(antiasthmatic activity of)

RN 112666-96-3 HCPLUS

L5 ANSWER 105 OF 163 HCPLUS COPYRIGHT 2002 ACS

1987:628857 Document No. 107:228857 New xanthine derivatives with potent and long lasting anti-bronchoconstrictive activity. Regnier, Gilbert L.; Guillonneau, Claude G.; Duhault, Jacques L.; Tisserand, Francoise P.; Saint-Romas, Guy; Holstorp, Sophie M. (Chem. Res. Dep., Inst. Rech. Servier, Suresnes, 92150, Fr.). European Journal of Medicinal Chemistry, 22(3), 243-50 (English) 1987. CODEN: EJMCA5. ISSN: 0223-5234. OTHER SOURCES: CASREACT 107:228857.

GI



AB Twenty-nine new derivs. of 8-aminoalkyl-substituted xanthine [e.g. I, R1 = H, Me, Et; R2 = Me, iso-Pr, Ph, etc.; R3 = H, Me, 2,3-dihydroxypropyl, etc.; R4 = H or F; and X = CH(OH)CH<sub>2</sub>, (CH<sub>2</sub>)<sub>n</sub>; n = 1-3] were synthesized. All I demonstrated a potent anti-bronchoconstrictive effect in the guinea pig and some had a very long duration of action (> 48h). II was selected for clin. trials in asthmatic patients because of its long duration of action, its lack of central nervous system-stimulating effects and its inhibiting action on mast cell degranulation and phosphodiesterase activity. Structure-activity relationships are discussed.

IT 90749-33-0P 90749-57-8P 90773-95-8P

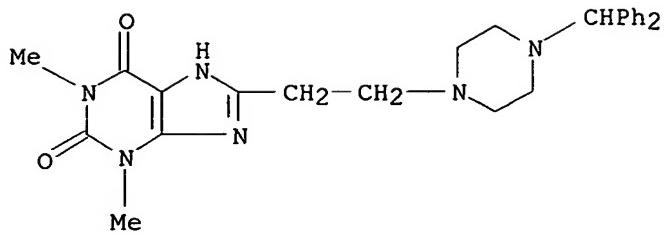
110480-49-4P 110480-52-9P 110480-53-0P

RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

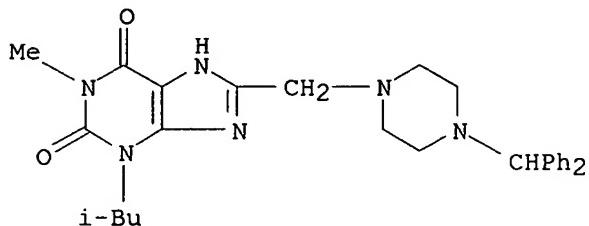
(prepn. and bronchodilating activity and toxicity of)

RN 90749-33-0 HCPLUS

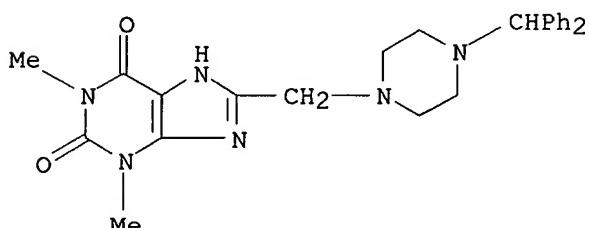
CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



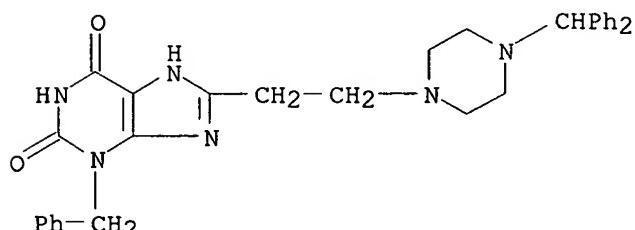
RN 90749-57-8 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(4-(diphenylmethyl)-1-piperazinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



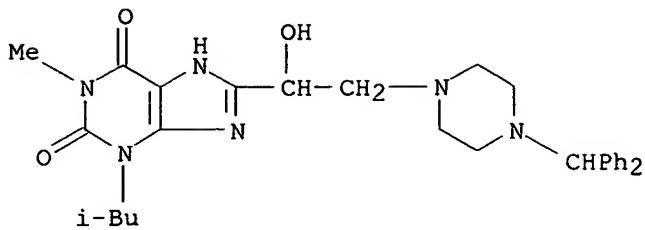
RN 90773-95-8 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(4-(diphenylmethyl)-1-piperazinyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 110480-49-4 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(2-[(4-(diphenylmethyl)-1-piperazinyl)ethyl]-3,7-dihydro-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

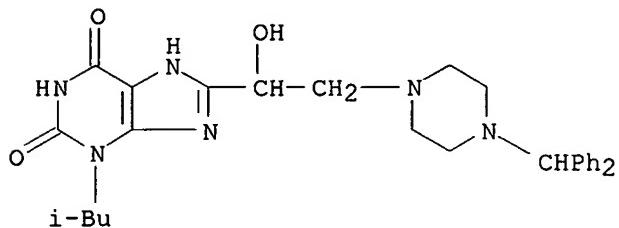


RN 110480-52-9 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[(2-[(4-(diphenylmethyl)-1-piperazinyl)-1-hydroxyethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 110480-53-0 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]-1-hydroxyethyl]-3,7-dihydro-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



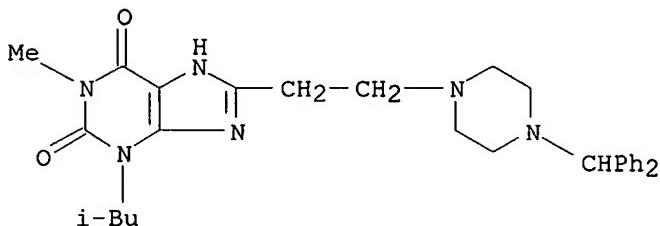
IT 90749-32-9P 90749-42-1P 110480-48-3P

110480-57-4P 110480-58-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. and bronchodilating and cAMP phosphodiesterase-inhibiting  
activity and toxicity of)

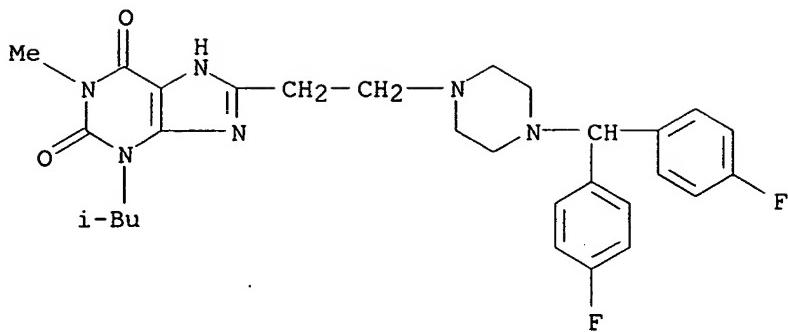
RN 90749-32-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)

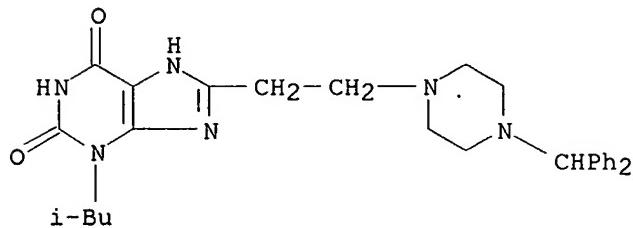


RN 90749-42-1 HCAPLUS

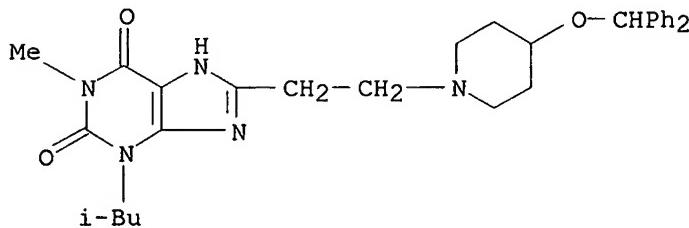
CN 1H-Purine-2,6-dione, 8-[2-[4-[bis(4-fluorophenyl)methyl]-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



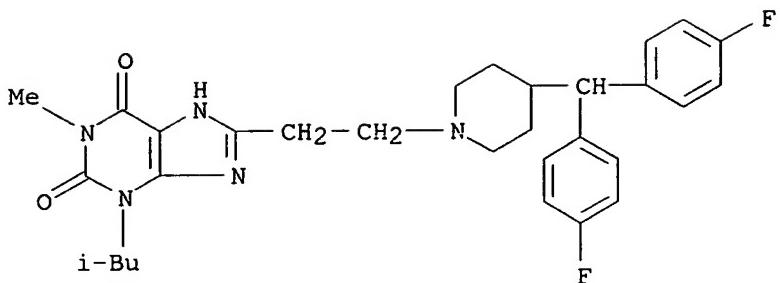
RN 110480-48-3 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 110480-57-4 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 110480-58-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-[bis(4-fluorophenyl)methyl]-1-piperidinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 106 OF 163 HCPLUS COPYRIGHT 2002 ACS

1987:440250 Document No. 107:40250 2-.beta.-D-Ribofuranosylbenzoxazole from 2,5-anhydro-D-allonoimide, and 1,3-dimethyl-8-.beta.-D-ribofuranosylxanthine from 2,5-anhydro-D-allono-thioimidates and -dithioates. El Khadem, Hassan S.; Kawai, Joshua (Dep. Chem., American Univ., Washington, DC, 20016, USA). Carbohydrate Research, 153(2), 271-83 (English) 1986. CODEN: CRBRAT. ISSN: 0008-6215. OTHER SOURCES: CASREACT 107:40250.

GI

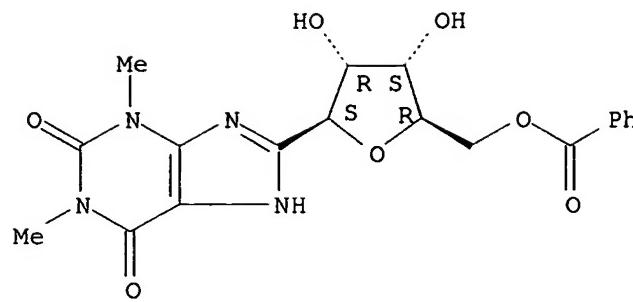
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The ability of imides, thioimidates, and dithioates to react with o-aminophenol (I) and 5,6-diamino-1,3-dimethyluracil (II) was studied using non-saccharide model compds., as well as saccharide derivs. All of the model compds. gave 2-methylbenzoxazole, but only Et bisthioacetate gave a purine deriv. with II. Anhydro-D-allonoimide III reacted with I to yield 2-.beta.-D-ribofuranosylbenzoxazole (IV), but failed to react with II. On reaction with II such fully acylated thioimidates as Et and benzyl 2,5-anhydrotri-O-benzoyl- or tri-O-p-toluoyl-D-allonothioimide hydrochloride yielded amidines that underwent aromatization of the furanose ring. Such monoacylated thioimidates as Et 2,5-anhydro-6-O-benzoyl-D-allonothiomidate hydrochloride yielded, with II, 8-(5-O-benzoyl-.beta.-D-ribofuranosyl)-1,3-dimethylxanthine, without aromatization. Such dithioates as benzyl and Et 2,5-anhydro-6-O-benzoyl-D-allonodithioate were obtained by treating the corresponding thioimidate with H<sub>2</sub>S in pyridine. With II, the second yielded 8-(5-O-benzoyl-.beta.-D-ribofuranosyl)-1,3-dimethylxanthine, which afforded the free C-nucleoside V on treatment with NH<sub>3</sub>-MeOH.

IT 108967-26-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prep. and debenzylation of)

RN 108967-26-6 HCPLUS  
CN 1H-Purine-2,6-dione, 8-(5-O-benzoyl-.beta.-D-ribofuranosyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

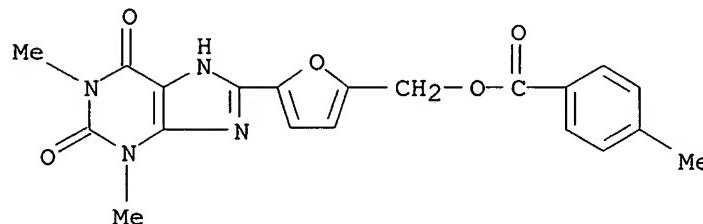


IT 108967-25-5P 108967-27-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 108967-25-5 HCPLUS

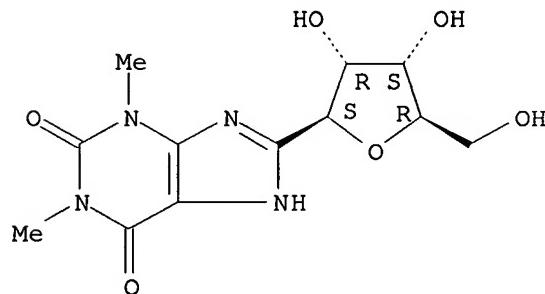
CN Benzoic acid, 4-methyl-, [5-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-2-furanyl]methyl ester (9CI) (CA INDEX NAME)



RN 108967-27-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-.beta.-D-ribofuranosyl- (9CI) (CA INDEX NAME)

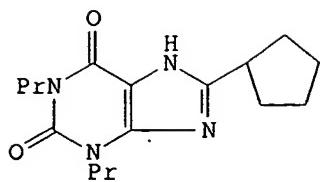
Absolute stereochemistry.



L5 ANSWER 107 OF 163 HCPLUS COPYRIGHT 2002 ACS

1987:400259 Document No. 107:259 Potent adenosine receptor antagonists that are selective for the A1 receptor subtype. Martinson, Elizabeth A.; Johnson, Roger A.; Wells, Jack N. (Sch. Med., Vanderbilt Univ., Nashville, TN, 37232, USA). Molecular Pharmacology, 31(3), 247-52 (English) 1987. CODEN: MOPMA3. ISSN: 0026-895X.

GI



AB A systematic study of xanthine structure-activity relationships that compared antagonist potency at the A1 receptor of adipocytes with potency at the A2 receptor of platelets was conducted. Since adenosine receptors are coupled to adenylate cyclase in these tissues, inhibition of adenylate cyclase via A1 receptors and stimulation via A2 receptors were used as models of receptor activation. Antagonist potency was quantitated by Schild anal., which yields an est. of affinity ( $K_i$ ) for the drug-receptor interaction.  $K_i$  Values of a series of xanthine analogs made it possible to identify structural modifications than enhanced antagonist selectivity for one receptor subtype over the other. Changes in the substituent at position 8 of the xanthine nucleus influenced antagonist potency at the A1 adenosine receptor more than at the A2 receptor. In particular, an 8-cyclohexyl or 8-cyclopentyl substituent promoted antagonist selectivity for the A1 receptor subtype. Thus, 1,3-dipropyl-8-cyclopentylxanthine (I) had comparatively high affinity ( $K_i = 0.47$  nM) at the A1 receptor, and was roughly 150-fold more potent as an antagonist of the A1- than of the A2-adenosine receptor subtype. In addn., the cycloalkylxanthines were relatively ineffective as inhibitors of cyclic nucleotide phosphodiesterase when used at concns. that produce marked adenosine receptor antagonism.

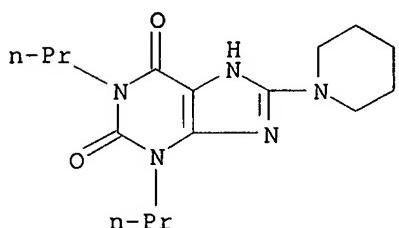
IT 108653-57-2 108653-58-3 108653-59-4

RL: BIOL (Biological study)

(A1- and A2-adenosine receptors antagonism by, structure in relation to)

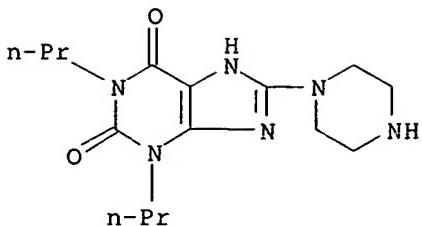
RN 108653-57-2 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-piperidinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)

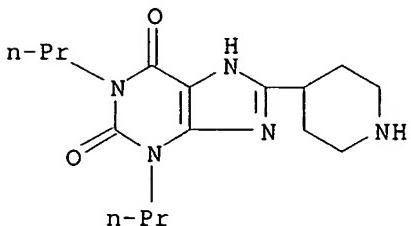


RN 108653-58-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1-piperazinyl)-1,3-dipropyl- (9CI)  
(CA INDEX NAME)



RN 108653-59-4 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(4-piperidinyl)-1,3-dipropyl- (9CI)  
 (CA INDEX NAME)

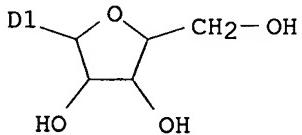
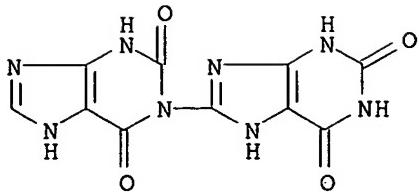


L5 ANSWER 108 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1987:109844 Document No. 106:109844 Electrochemical oxidation of xanthosine.  
 Tyagi, S. K.; Dryhurst, Glenn (Dep. Chem., Univ. Oklahoma, Norman, OK,  
 73019, USA). Journal of Electroanalytical Chemistry and Interfacial  
 Electrochemistry, 216(1-2), 137-56 (English) 1987. CODEN: JEIEBC. ISSN:  
 0022-0728.

AB The electrochem. oxidn. of xanthosine [146-80-5] in aq. soln. at pH 2.0 on a pyrolytic graphite electrode was studied. The primary electrochem. oxidn. reaction is an irreversible 1-electron, 1-H<sup>+</sup> reaction giving the C(8).ovrhdot. free radical. To account for the ultimate products formed, the latter primary radical reacts with xanthosine to give at least 1 N.ovrhdot. free radical and with H<sub>2</sub>O to give an 8-hydroxylated free radical. The C(8).ovrhdot. and N.ovrhdot. radicals couple to give a xanthosylxanthosine dimer which rapidly loses 1 ribosyl residue to give a xanthosylxanthine dimer. The 8-hydroxylated radical reacts with the C(8).ovrhdot. and N.ovrhdot. radicals to give 2 isomeric hydroxylated xanthosylxanthosines. The 8-hydroxylated radical can also undergo further electrochem. oxidn. (1 e-, 1 H<sup>+</sup>) to 9-.beta.-D-ribofuranosyluric acid which is immediately oxidized (2 e-, 2 H<sup>+</sup>) to a very reactive quinonoid. Attack by H<sub>2</sub>O on the quinonoid gives 2 isomeric tertiary alc. intermediates which were isolated and characterized by UV and mass spectra and by their reaction with H<sub>2</sub>O to give a diol.

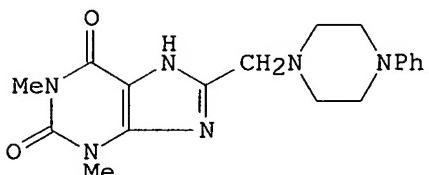
IT 107137-56-4P  
 RL: FORM (Formation, nonpreparative); PREP (Preparation)  
 (formation of, by electrochem. oxidn. of xanthosine on pyrolytic  
 graphite anode in aq. soln.)

RN 107137-56-4 HCPLUS  
 CN Xanthosine, (2,3,6,7-tetrahydro-2,6-dioxo-1H-purinyl)- (9CI) (CA INDEX  
 NAME)



L5 ANSWER 109 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
 1987:67011 Document No. 106:67011 8-[4-(Phenyl-1-piperazinyl)methyl]theophylline. Danila, Gheorghe; Cojocaru, Zenaida; Nechifor, Mihai; Dorneanu, Vasile (Institutul de Medicina si Farmacie, Rom.). Rom. RO 88944 B1 19860331, 2 pp. (Romanian). CODEN: RUXXA3.  
 APPLICATION: RO 1984-113558 19840209.

GI



I

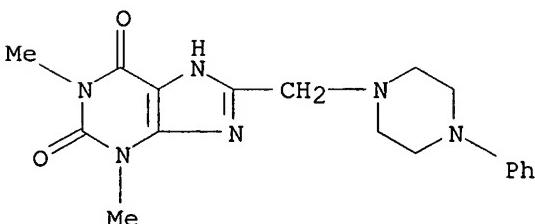
AB The title compd. I having therapeutic properties (no data) was prep'd. Thus, theophylline, N-phenylpiperazine, HCHO (35%), and EtOH were refluxed for 30 h and the mixt. cooled and pptd. with petroleum ether to give I. I is a white substance insol. in EtOH, MeOH, PrOH, and benzene but sol. in CHCl<sub>3</sub>, CH<sub>2</sub>C<sub>12</sub> and in hot EtOH, PrOH and acetone.

IT 106585-73-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

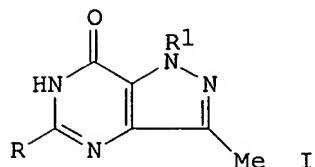
RN 106585-73-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(4-phenyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 110 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1987:50155 Document No. 106:50155 Synthesis and structure-activity relationships of pyrazolo[4,3-d]pyrimidin-7-ones as adenosine receptor antagonists.- Hamilton, Harriet W.; Ortwine, Daniel F.; Worth, Donald F.; Bristol, James A. (Dep. Chem., Warner-Lambert/Parke-Davis Pharm. Res., Ann Arbor, MI, 48105, USA). Journal of Medicinal Chemistry, 30(1), 91-6 (English) 1987. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 106:50155.

GI



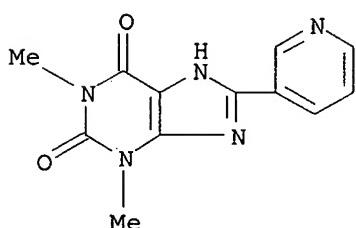
AB A series of 21 1,3-dialkylpyrazolo[4,3-d]pyrimidin-7-ones, e.g., I ( $R = 2\text{-MeOC}_6\text{H}_4$ ,  $R1 = \text{Me}$ ), substituted in the 5-position with various Ph substituents, was prep'd. and found to have affinity for the adenosine A<sub>1</sub> receptor. The potency pattern due to substituents on the Ph ring was parallel that found in a previously reported (1985) 1,3-dialkyl-8-phenylxanthine series. A quant. structure-activity relationship was developed between these two series that correctly predicted the potencies of six addnl. I. Using the correlation as a guide, I ( $R = 4\text{-Me}_2\text{NCH}_2\text{CH}_2\text{NSO}_2\text{C}_6\text{H}_4$ ,  $R1 = \text{Me}$ ), having improved aq. solv., was prep'd. It is hypothesized that I and analogously substituted xanthines fit the adenosine receptor in an analogous fashion.

IT 1029-62-5 1088-64-8

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (adenosine receptor binding activity of, pyrazolopyrimidine analog binding affinity in relation to)

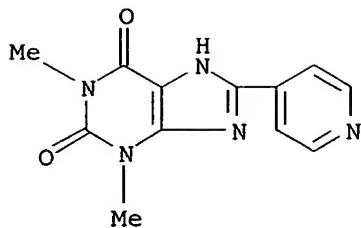
RN 1029-62-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 1088-64-8 HCPLUS

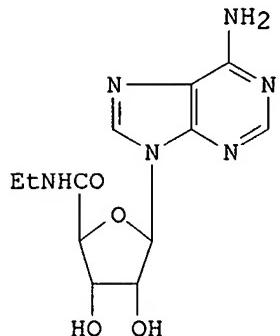
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 111 OF 163 HCPLUS COPYRIGHT 2002 ACS

1986:419132 Document No. 105:19132 Characterization of the A2 adenosine receptor labeled by [<sup>3</sup>H]NECA in rat striatal membranes. Bruns, Robert F.; Lu, Gina H.; Pugsley, Thomas A. (Dep. Pharmacol., Warner-Lambert/Parke-Davis Pharm. Res., Ann Arbor, MI, 48105, USA). Molecular Pharmacology, 29(4), 331-46 (English) 1986. CODEN: MOPMA3. ISSN: 0026-895X.

GI



I

AB To study the putative A2 component of <sup>3</sup>H-labeled NECA (I) [35920-39-9] binding, several compds. were exampd. for the ability to selectively eliminate the A1 component of binding in rat striatal membranes; N6-cyclopentyladenosine [41552-82-3] gave the most satisfactory results. Binding of [<sup>3</sup>H]NECA in the presence of 50 nM N6-cyclopentyladenosine was characterized. The rank order of potency for inhibition of [<sup>3</sup>H]NECA binding was NECA .mchgt. 2-chloroadenosine [146-77-0] > N6-[ (R)-1-methyl-2-phenylethyl]adenosine (R-PIA) [38594-96-6] > N6-cyclohexyladenosine [36396-99-3] > S-PIA [38594-97-7], indicating that binding was to an A2 adenosine receptor. When affinities of compds. in [<sup>3</sup>H]NECA binding to A2 receptors were compared to their affinities in [<sup>3</sup>H]N6-cyclohexyladenosine binding to A1 receptors, N6-cyclopentyladenosine was the most A1-sensitive agonist (A1 inhibition const. (Ki), 0.59 nM; A2Ki, 460 nM; Ki ratio, 780), whereas the selective coronary vasodilator 2-(phenylamino)adenosine [53296-10-9] was the most A2-selective agonist (A1, 560 nM; A2, 120 nM; ratio, 0.21). The antagonist 8-cyclopentyltheophylline had considerable A1 selectivity (A1, 11 nM; A2, 1400 nM; ratio, 130), whereas alloxazine had slight A2 selectivity (A1, 5200 nM; A2, 2700; ratio, 0.52). [<sup>3</sup>H]NECA binding to A2 receptors was highest in striatum but was detectable at much lower levels in each of 7 other brain areas. The regional distribution of [<sup>3</sup>H]NECA binding and the affinities of adenosine agonists and antagonists for

inhibition of binding indicate that the site labeled by [3H]NECA belongs to the high-affinity, or A2a, subclass of A2 receptor.

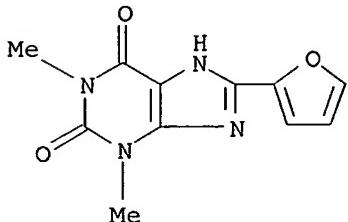
IT 33797-74-9

RL: BIOL (Biological study)

(purinergic A1 and A2 receptors binding of, in brain membranes,  
structure in relation to)

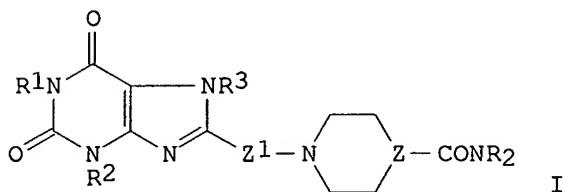
RN 33797-74-9 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA  
INDEX NAME)



1985:578277 Document No. 103:178277 Xanthine derivatives and pharmaceutical compositions containing them. Regnier, Gilbert; Guillonneau, Claude; Duhault, Jacques; Roman, Francois (ADIR, Fr.). Eur. Pat. Appl. EP 149578 A2 19850724, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE. (French). CODEN: EPXXDW. APPLICATION: EP 1985-400072 19850116. PRIORITY: FR 1984-659 19840117.

GI



AB 8-Substituted xanthines I [R = alkyl, NR2 form a heterocycle; Z = N, CHNH; Z1 = (CH2)n (n = 1,2,3,4), hydroxyalkylene; R1 = H, alkyl; R2 = H, alkyl, alkenyl, PhCH2; R3 = H, Me], which were prepd., are useful in the treatment of migraine and asthenia (no data). 8-(3-Bromopropyl)-1,3,7-trimethylxanthine was treated with 1-(diethylcarbamoyl)piperazine to give I [R = Et, Z = N, Z1 = (CH2)3, R1 = R2 = R3 = Me].

IT 98833-98-8 98833-99-9 98834-03-8

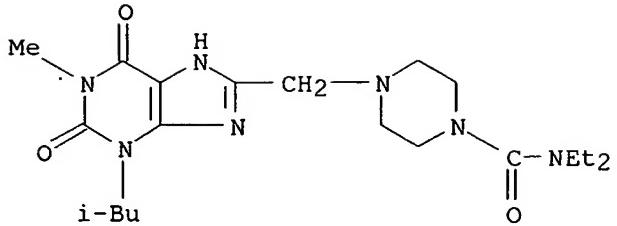
98834-09-4 98834-10-7 98834-11-8

98834-12-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
(hydrogenolysis of)

RN 98833-98-8 HCAPLUS

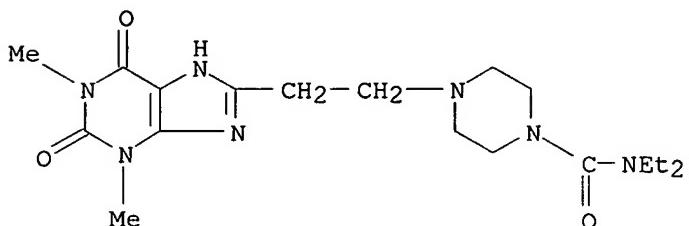
CN 1-Piperazinecarboxamide, N,N-diethyl-4-[[2,3,6,7-tetrahydro-1-methyl-3-(2-methylpropyl)-2,6-dioxo-1H-purin-8-yl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

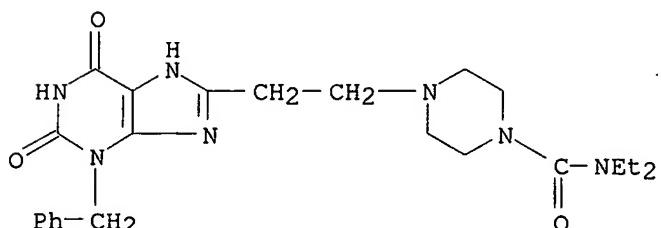
RN 98833-99-9 HCAPLUS

CN 1-Piperazinecarboxamide, N,N-diethyl-4-[2-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)ethyl]- (9CI) (CA INDEX NAME)



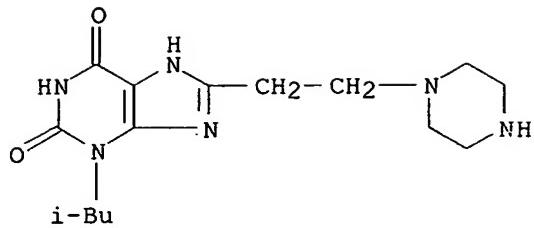
RN 98834-03-8 HCAPLUS

CN 1-Piperazinecarboxamide, N,N-diethyl-4-[2-[2,3,6,7-tetrahydro-2,6-dioxo-3-(phenylmethyl)-1H-purin-8-yl]ethyl]- (9CI) (CA INDEX NAME)



RN 98834-09-4 HCAPLUS

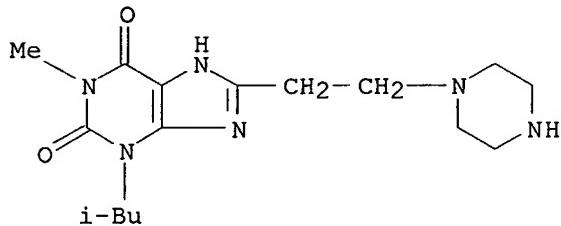
CN 1H-Purine-2,6-dione, 3,7-dihydro-3-(2-methylpropyl)-8-[2-(1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 98834-10-7 HCAPLUS

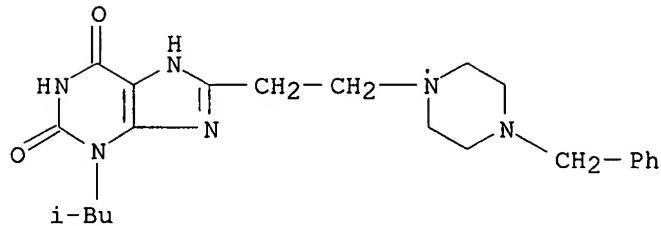
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-(2-methylpropyl)-8-[2-(1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

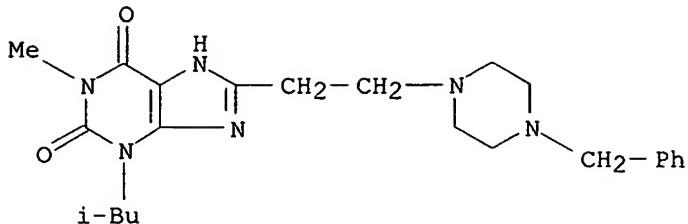
RN 98834-11-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-(2-methylpropyl)-8-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 98834-12-9 HCAPLUS

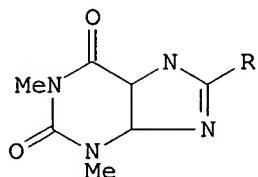
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-(2-methylpropyl)-8-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



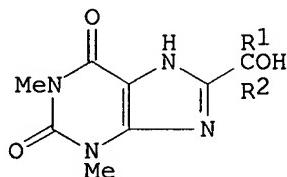
L5 ANSWER 113 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1985:522645 Document No. 103:122645 Photochemistry of purine systems, IV. Photoreactions of theophylline with ethers in the presence of aliphatic ketones. Erndt, Aleksander; Para, Andrzej; Kostuch, Andrzej; Fiedorowicz, Maciej (Dep. Chem. Phys., Hugo Kollataj Acad. Agric., Krakow, PL-30059, Pol.). Liebigs Annalen der Chemie (5), 937-43 (English) 1985. CODEN: LACHDL. ISSN: 0170-2041. OTHER SOURCES: CASREACT 103:122645.

GI



I



II

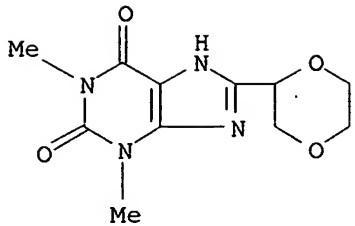
AB Inadn. (.lambda. >290 nm) of theophylline in a mixt. of ether-ketone [e.g. acetone-(Me<sub>2</sub>CH)<sub>2</sub>O] gave products I [R = Me(OEt)CH, Pr(OMe)CH, PrOCH<sub>2</sub>, Et(PrO)CH, (Me<sub>2</sub>CHO)Me<sub>2</sub>C, etc.] and II (R<sub>1</sub>,R<sub>2</sub> given: Me, Me; Me, Et; Me, Pr). The reactions involve substitution of theophylline with the .alpha.-position of ethers. Each cyclic ether and sym. open-chain ether gave exclusively one etheral deriv. of theophylline, whereas in the case of an unsym. ether two products were obtained due to an attack of each of the .alpha.-C atoms. Each reaction afforded quite appreciable quantities of products II (R<sub>1</sub>,R<sub>2</sub> as above) formed by a path involving an attack of intermediate ketyl radicals R<sub>1</sub>C··(OH)R<sub>2</sub> at theophylline position 8. The reaction proceeds via excitation of the ketonic singlet-singlet (S<sub>0</sub>-S<sub>1</sub>) transition decay to the carbonyl triplet (S<sub>1</sub>-T<sub>1</sub>) which abstrs. a H atom from the .alpha.-C of the ether to form an other radical and a ketyl radical.

IT 66274-13-3P 66274-14-4P 66274-15-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

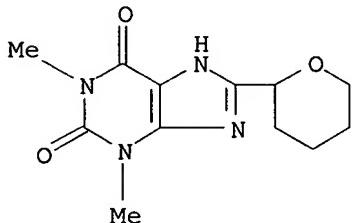
RN 66274-13-3 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(1,4-dioxan-2-yl)-3,7-dihydro-1,3-dimethyl- (9CI)  
(CA INDEX NAME)



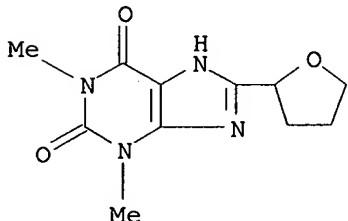
RN 66274-14-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2H-pyran-2-yl)- (9CI) (CA INDEX NAME)



RN 66274-15-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2-furanyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 114 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1985:128355 Document No. 102:128355 Assay techniques utilising specific binding agents. Hill, Hugh Allen Oliver (Genetics International, Inc., USA). Eur. Pat. Appl. EP 125139 A2 19841114, 97 pp. DESIGNATED STATES: R: BE, CH, DE, FR, GB, IT, LI, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1984-303090 19840508. PRIORITY: GB 1983-12263 19830505; GB 1983-12259 19830505; GB 1983-12265 19830505; GB 1983-25316 19830921; GB 1983-33650 19831216; GB 1983-33651 19831216; GB 1984-1399 19840119; GB 1984-5262 19840229; GB 1984-5263 19840229.

AB Specific binding reagents and electrochem. enzyme immunoassay (homogeneous or heterogeneous) techniques are described for the detn. of complex biol. mols. (free or in mixts.) such as ligands, haptens, or antigens and for DNA or RNA sequencing and other types of reactions involving specific nonimmunol. binding. The binding reaction is carried out in assocn. with an enzyme-mediator system electrochem. linked to a substrate so that the binding reaction affects the electrochem. availability of 1 of the components and is detected by the electrode. Thus, theophylline was detd. by electrochem. enzyme immunoassay by using a ferrocene-theophylline

conjugate and antiferrocene antibodies. If theophylline is present in the sample, it competes with the ferrocene-drug conjugate for its antibody, thus preventing the binding of the ferrocene conjugate and leaving it free to mediate between glucose oxidase and the electrode. Std. curves were obtained for theophylline in the therapeutic range of interest (0-40 .mu.g/mL).

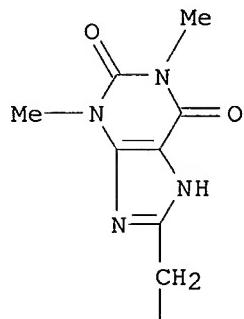
IT 95461-78-2P

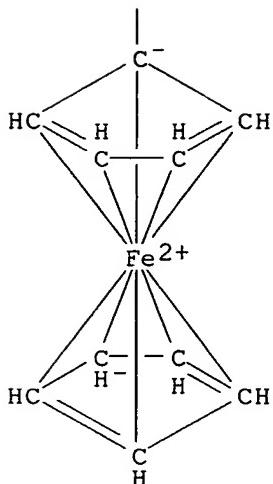
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 95461-78-2 HCPLUS

CN Ferrocene, [(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A





L5 ANSWER 115 OF 163 HCAPLUS COPYRIGHT 2002 ACS

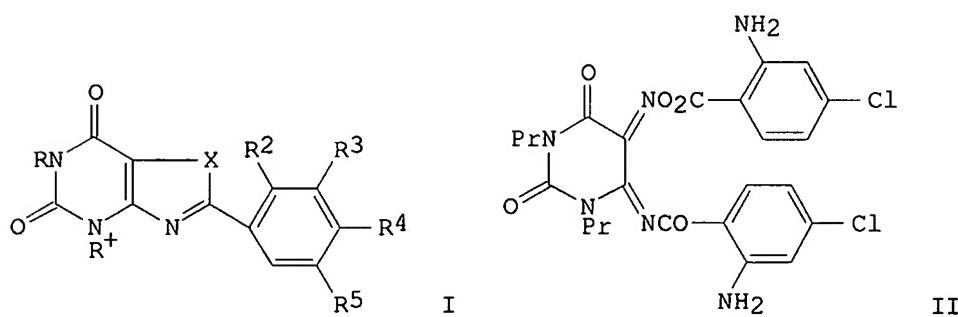
1985:6061 Document No. 102:6061 Antagonists for adenosine receptors.

Snyder, S. H.; Daly, J. W.; Bruns, R. F. (John Hopkins University, USA).

Belg. BE 898946 A1 19840618, 39 pp. (French). CODEN: BEXXAL.

APPLICATION: BE 1984-212418 19840217. PRIORITY: US 1983-467894 19830218.

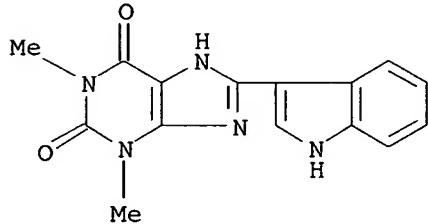
GI



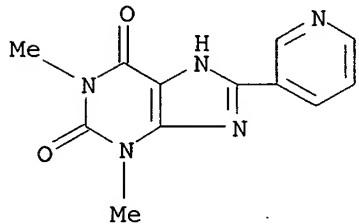
AB Xanthine derivs. I [X = NH, O, S; R = allyl, (un)substituted alkyl, cycloalkyl; R1 = H, allyl, (un)substituted alkyl, cycloalkyl; R2 = NH2, OH; R3, R5 = H, halogen, alkyl, alkoxy, OH, NO2, NH2; R4 = halogen, (un)substituted alkyl, Ph, amino, cycloalkyl, OH, CO2H, alkoxy, cycloalkoxy] were prep'd. Thus 4,2-Cl(O2N)C6H3CO2H were treated with 1,3-dipropyl-5-nitroso-6-aminouracil and the resulting diimine II reduced with (NH4)2S to give I (X = NH, R = R1 = Pr; R2 = NH2, R3 = R5 = H, R4 = Cl, III). III had a cyclohexyladenosine antagonist ED50 of 0.05 nM in vitro. Cyclohexyladenosine antagonist data are give for >90 I and structure-activity relationships are discussed.

IT 970-84-3 1029-62-5 1088-64-8 1088-65-9  
33797-74-9 33797-75-0 93214-93-8  
93214-94-9 93214-95-0 93215-03-3  
93240-07-4

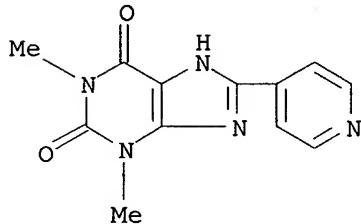
RL: RCT (Reactant); RACT (Reactant or reagent)  
(adenosine antagonist activity of)  
RN 970-84-3 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1H-indol-3-yl)-1,3-dimethyl- (9CI)  
(CA INDEX NAME)



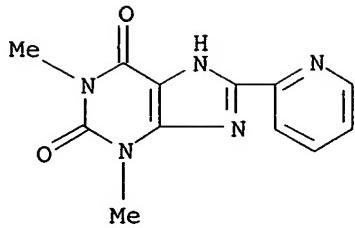
RN 1029-62-5 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



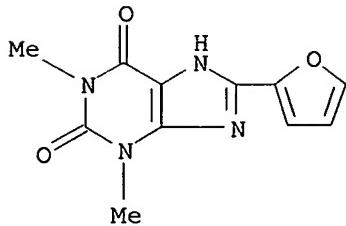
RN 1088-64-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



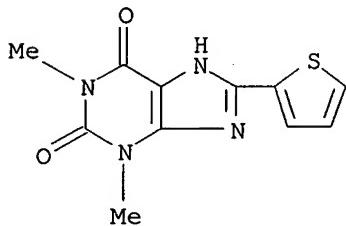
RN 1088-65-9 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-pyridinyl)- (9CI) (CA INDEX NAME)



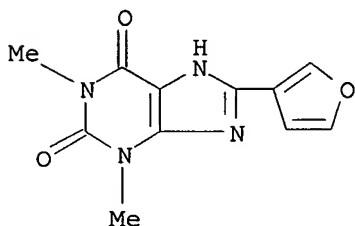
RN 33797-74-9 HCPLUS  
CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



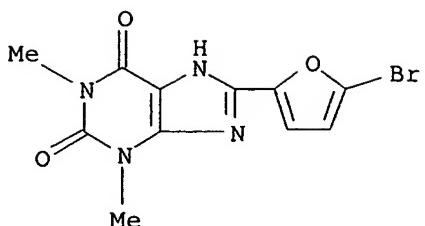
RN 33797-75-0 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



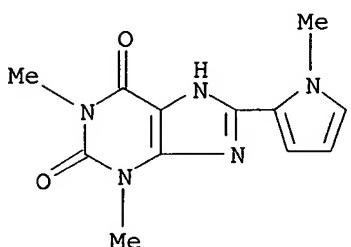
RN 93214-93-8 HCPLUS  
CN 1H-Purine-2,6-dione, 8-(3-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



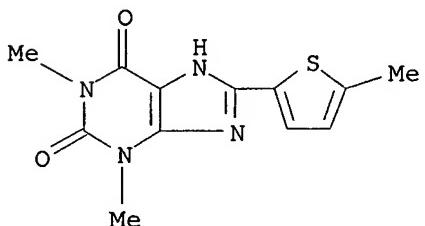
RN 93214-94-9 HCPLUS  
CN 1H-Purine-2,6-dione, 8-(5-bromo-2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



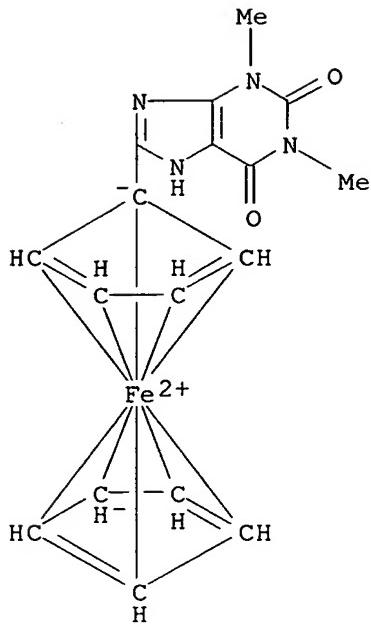
RN 93214-95-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-methyl-1H-pyrrol-2-yl)-  
(9CI) (CA INDEX NAME)



RN 93215-03-3 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(5-methyl-2-thienyl)-  
(9CI) (CA INDEX NAME)



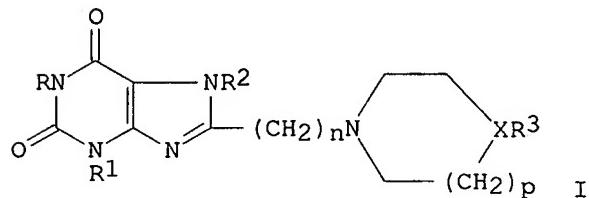
RN 93240-07-4 HCAPLUS  
CN Ferrocene, (2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-  
(9CI) (CA INDEX NAME)



L5 ANSWER 116 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1984:490670 Document No. 101:90670 Xanthine derivatives and pharmaceutical compositions containing them. Regnier, Gilbert; Guillonneau, Claude; Duhaulat, Jacques; Boulanger, Michelle (ADIR, Fr.). Fr. Demande FR 2531085 A1 19840203, 20 pp. (French). CODEN: FRXXBL. APPLICATION: FR 1982-13155 19820728.

GI



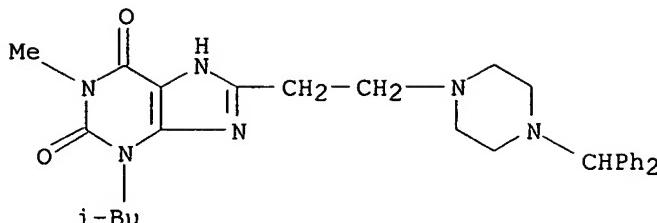
AB Xanthines I [R = alkyl; R1 = (un)substituted alkyl; R2 = H, alkyl, hydroxyalkyl, dihydroxyalkyl; R3 = CH(C6H4R4)2, CH2CH:CHC6H4R4; R4 = H, halogen, alkyl, alkoxy; X = N, CH, CHO, CHNR1, aminoalkylaminomethylene; n = 1-5; p = 0-2], useful as bronchodilators, were prepd. Thus, I (R = Me, R1 = CH2CHMe2, R2 = H, R3 = CHPh2, X = N, n = 2, p = 1) (II) was prepd. from 6-amino-1-isobutyl-3-methyluracil in 6 steps via the 5,6-diaminouracil, its methoxypropionyl deriv., and the bromoethylxanthine. II had ED60 on A2 purinergic receptors of 15 .mu.M.

IT 90749-32-9P

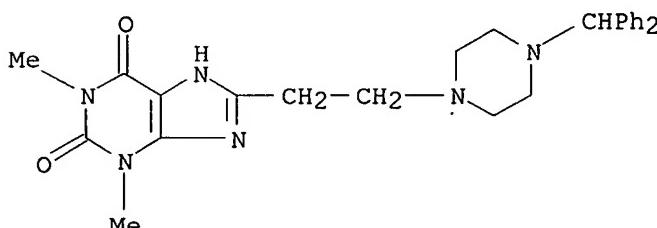
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and bronchodilator activity of)

RN 90749-32-9 HCAPLUS

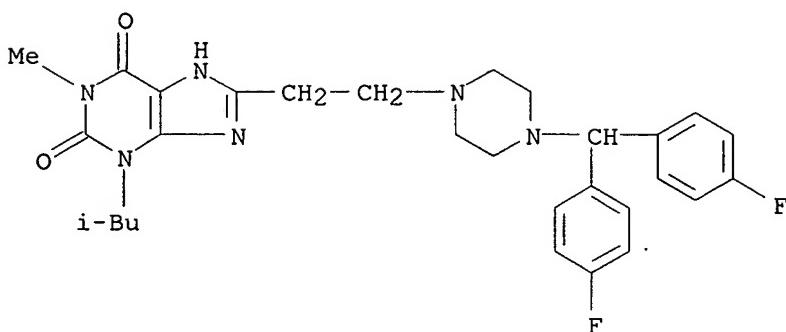
CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



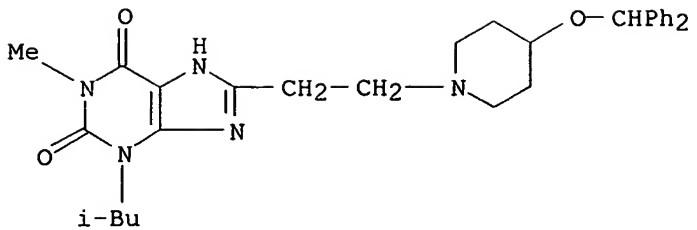
IT 90749-33-0P 90749-42-1P 90749-52-3P  
 90749-57-8P 90749-58-9P 90773-95-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 90749-33-0 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethyl)-1-piperazinyl]ethyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 90749-42-1 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-[bis(4-fluorophenyl)methyl]-1-piperazinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



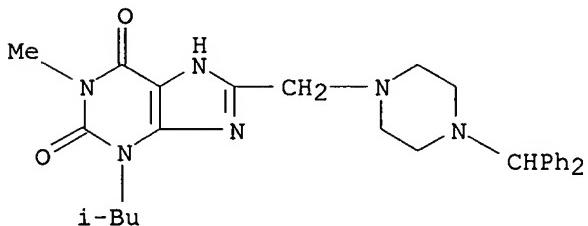
RN 90749-52-3 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-[2-[4-(diphenylmethoxy)-1-piperidinyl]ethyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

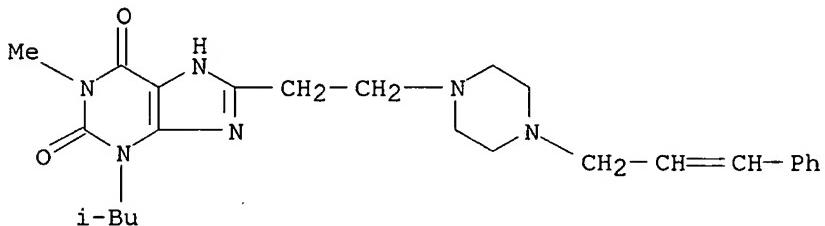
RN 90749-57-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(4-(diphenylmethyl)-1-piperazinyl)methyl]-3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



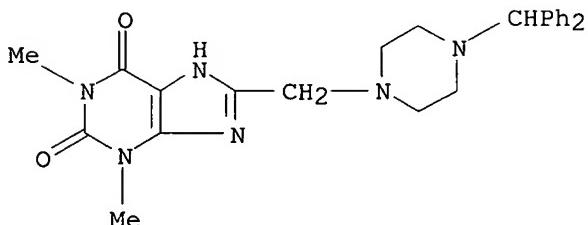
RN 90749-58-9 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-(2-methylpropyl)-8-[2-[4-(3-phenyl-2-propenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 90773-95-8 HCPLUS

CN 1H-Purine-2,6-dione, 8-[(4-(diphenylmethyl)-1-piperazinyl)methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



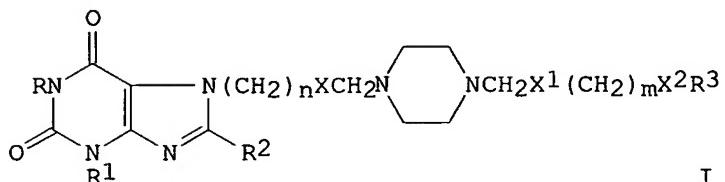
L5 ANSWER 117 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1983:470479 Document No. 99:70479 Piperazine derivatives of theophylline.

Favier, Colette; Pinhas, Henri; Beranger, Serge; Pascal, Jean Claude  
(Laroche Navarron S. A., Fr.). Eur. Pat. Appl. EP 72307 A1 19830216, 37  
pp. DESIGNATED STATES: R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE.  
(English). CODEN: EPXXDW. APPLICATION: EP 1982-401445 19820730.

PRIORITY: US 1981-288836 19810731.

GI



I

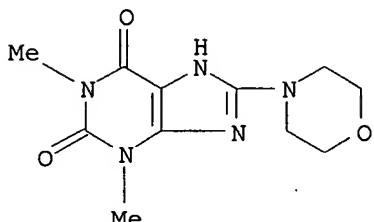
AB Antihistaminic (no data) title compds. I ( $X, X_1 = \text{CH}_2, \text{CHOH}$ , esterified  $\text{CHOH}, \text{CO}$ ;  $X_2 = \text{O}, \text{S}$ ;  $R, R_1 = \text{alkyl}$ ;  $R_2 = \text{H, amino}$ ;  $R_3 = \text{Ph, substituted Ph}$ ;  $m, n = 0-4$ ) were prep'd. Thus, I ( $X = \text{CHOH}, X_1 = \text{CH}_2, X_2 = \text{S}, R = \text{Me}$ ,  $R_1 = \text{CH}_2\text{CHMe}_2$ ,  $R_2 = \text{morpholino}$ ,  $R_3 = \text{Ph}$ ,  $m = n = 1$ ) was prep'd. by treating the corresponding chloro(hydroxy)propyltheophylline with the phenylthiopropylpiperazine.

IT 30958-49-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and reaction of, with epichlorohydrin)

RN 30958-49-7 HCAPLUS

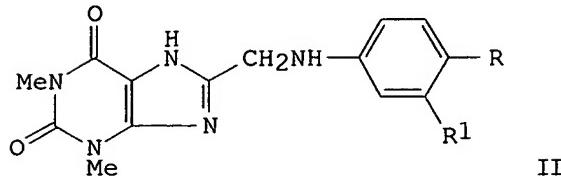
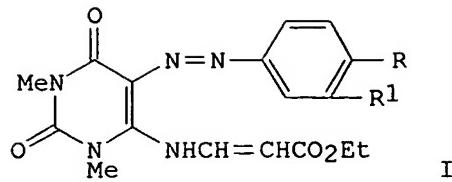
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- (9CI)  
(CA INDEX NAME)



L5 ANSWER 118 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1983:53498 Document No. 98:53498 A novel synthesis of theophylline derivatives. Yoneda, Fumio; Koga, Ryosuke (Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, 862, Japan). Journal of Heterocyclic Chemistry, 19(4), 813-16 (English) 1982. CODEN: JHTCAD. ISSN: 0022-152X.

GI



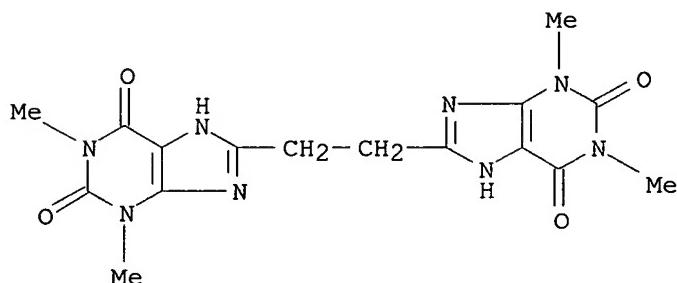
AB Treatment of 6-amino-5-arylazo-1,3-dimethyluracils with Et propiolate gave the corresponding Michael-type adducts I (R = H, Cl, Br, Me, MeO; R1 = H, Cl, Me, MeO), which on treatment with a mixt. of HCl and AcOH caused acid-catalyzed rearrangement accompanied with cyclization to give rise to the 8-anilinomethyltheophylline derivs. II (R = H, Cl, Br, Me; R1 = H, Cl, Me). When the arylazo group in I had an electron-releasing substituent as in I (R = MeO, R1 = H, MeO), the reaction proceeded in a different way to give 1,2-bis(theophyllin-8-yl)ethanes.

IT **1784-67-4P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 1784-67-4 HCPLUS

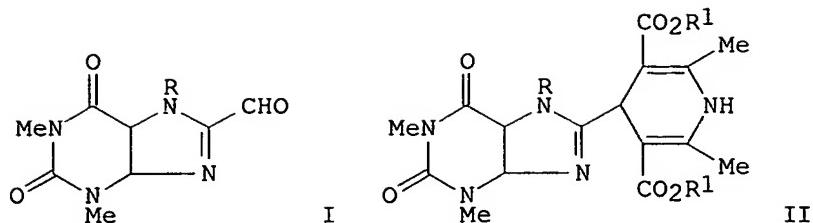
CN 1H-Purine-2,6-dione, 8,8'-(1,2-ethanediyl)bis[3,7-dihydro-1,3-dimethyl-  
(9CI) (CA INDEX NAME)



L5 ANSWER 119 OF 163 HCPLUS COPYRIGHT 2002 ACS

1981:620045 Document No. 95:220045 1,3-Dimethyl-8-formyl-7-substituted derivatives of xanthine in the Hantzsch synthesis. Jarymowicz, Barbara (Dep. Chem. Synth., Inst. Pharm. Ind., Warsaw, 01-793, Pol.). Acta Poloniae Pharmaceutica, 38(2), 201-5 (Polish) 1981. CODEN: APPHAX. ISSN: 0001-6837.

GI



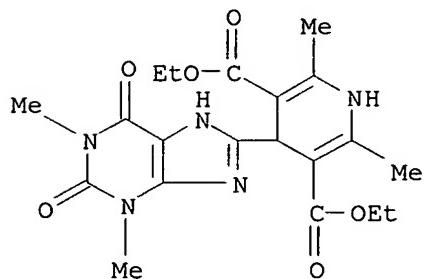
AB 8-Formyl derivs. (I, R = H, PhCH<sub>2</sub>, 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>) of xanthine were obtained in 67-81% yields by oxidn. of the corresponding hydroxymethyl compds. with Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> in AcOH. I heated with AcCH<sub>2</sub>CO<sub>2</sub>R<sub>1</sub> (R<sub>1</sub> = Me, Et) in alc. NH<sub>3</sub> gave II. II (R = H, R<sub>1</sub> = Et) treated with Me<sub>2</sub>SO<sub>4</sub> in aq. NaOH and with Br(CH<sub>2</sub>)<sub>2</sub>Br in DMF yielded II (R = Me and CH<sub>2</sub>CH<sub>2</sub>Br, resp.; R<sub>1</sub> = Et).

IT 79927-26-7P 79927-32-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

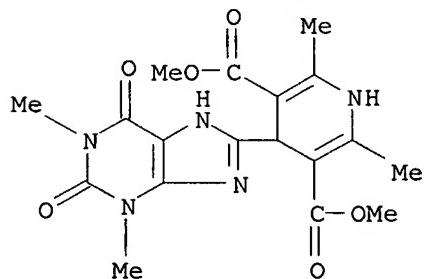
RN 79927-26-7 HCPLUS

CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, diethyl ester (9CI)  
(CA INDEX NAME)



RN 79927-32-5 HCPLUS

CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, dimethyl ester (9CI)  
(CA INDEX NAME)



L5 ANSWER 120 OF 163 HCPLUS COPYRIGHT 2002 ACS

1981:435269 Document No. 95:35269 Adenosine antagonism by purines,  
pteridines, and benzopteridines in human fibroblasts. Bruns, Robert F.

(Dep. Neurosci., Univ. California, La Jolla, CA, 92093, USA). Biochemical Pharmacology, 30(4), 325-33 (English) 1981. CODEN: BCPCA6. ISSN: 0006-2952.

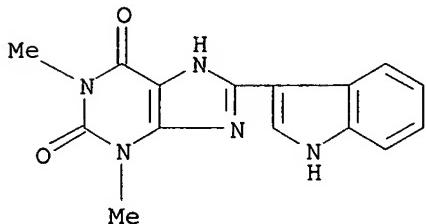
AB Testing of >100 purine bases and structurally related heterocycles as adenosine (I) [58-61-7] antagonists in VA13 fibroblasts (detd. by cAMP increase) yielded 3 families of I antagonists: xanthines, benzo[g]pteridines, and 9-substituted adenines. For the xanthines, the optimal group at the 1-position was Bu (5-fold improvement vs. Me), at the 7-position was 2-chloroethyl (5-fold improvement vs. H), and at the 8-position was p-bromophenyl (100-fold improvement vs. H). The receptors apparently had butyl- and phenyl-sized pockets at the 1- and 8-positions, resp., since compds. with larger groups had greatly reduced activity.

IT 970-84-3

RL: BIOL (Biological study)  
(adenosine receptor of fibroblast antagonism by)

RN 970-84-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1H-indol-3-yl)-1,3-dimethyl- (9CI)  
(CA INDEX NAME)

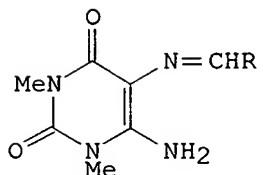


L5 ANSWER 121 OF 163 HCPLUS COPYRIGHT 2002 ACS

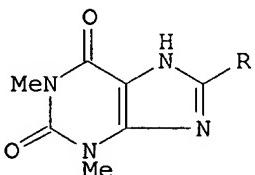
1981:121467 Document No. 94:121467 Studies on heterocyclic compounds.

XXXII. Synthesis of 8-substituted theophyllines from 6-amino-5-benzylideneamino-1,3-dimethyluracils with nickel peroxide. Mineo, Satoshi; Ogura, Haruo; Nakagawa, Kunio (Sch. Pharm. Sci., Kitasato Univ., Tokyo, 108, Japan). Chemical & Pharmaceutical Bulletin, 28(9), 2835-8 (English) 1980. CODEN: CPBTAL. ISSN: 0009-2363.

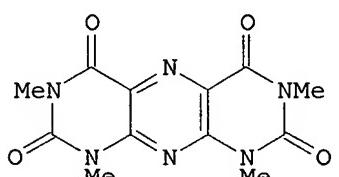
GI



I



II



III

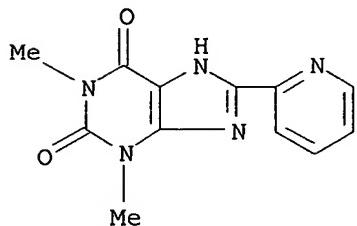
AB Oxidn. of 6-amino-5-benzylideneamino-1,3-dimethyluracils I (R = Ph, p-MeOC<sub>6</sub>H<sub>4</sub>, p-ClC<sub>6</sub>H<sub>4</sub>, p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, 2-pyridyl) with Ni peroxide in Me<sub>2</sub>SO afforded 8-substituted theophyllines II and Me<sub>2</sub>SO<sub>2</sub>. Ni peroxide oxidn. of the Schiff base acetate II [R = (CHOAc)<sub>4</sub>CH<sub>2</sub>OAc] did not give a nucleoside analog, but the pyrimidopteridinetetrone III and penta-O-acetylgluconic acid were obtained. The reaction mechanisms of nickel peroxide and the Schiff bases are discussed.

IT 1088-65-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepns. of)

RN 1088-65-9 HCPLUS

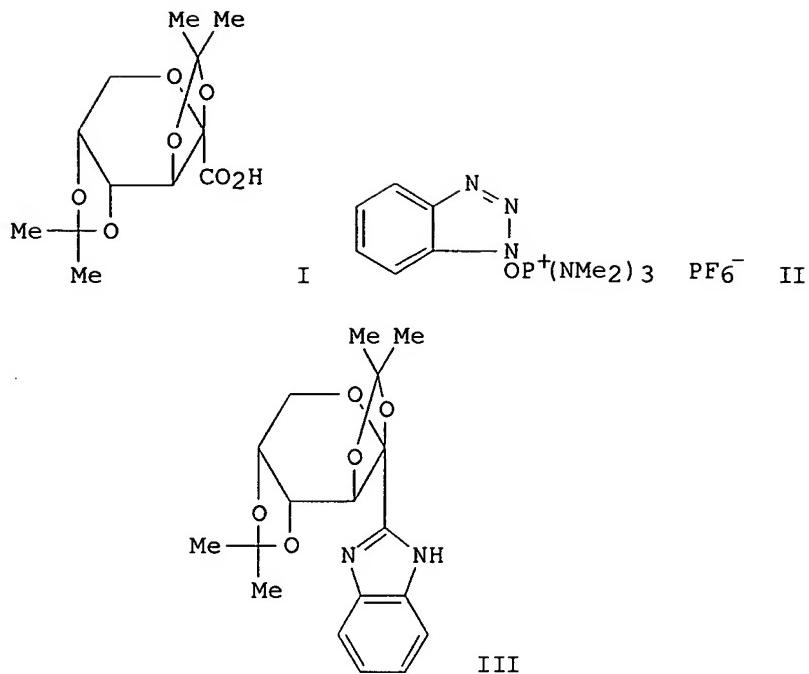
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-pyridinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 122 OF 163 HCPLUS COPYRIGHT 2002 ACS

1981:84425 Document No. 94:84425 Synthetic C-glycosyl nucleosides. A new approach. Chapleur, Yves; Castro, Bertrand (Lab. Chim. Org., Univ. Nancy I, Nancy, 54037, Fr.). Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (12), 2683-5 (English) 1980. CODEN: JCPRB4. ISSN: 0300-922X.

GI



AB Five C-nucleoside analogs were prep'd. from the hexulosonic acid I, easily obtained from fructose, by reaction with arom. diamines. E.g., I, 1.1 mol equiv o-phenylenediamine, and 1.1 mol equiv 'le BOP' coupling reagent II were dissolved in CH<sub>2</sub>Cl<sub>2</sub>, NEt<sub>3</sub> added, and after 5 min, work-up gave the crude coupled intermediate. This was dissolved in diglyme, Na<sub>2</sub>CO<sub>3</sub> added, and the mixt. heated at 160.degree. for 14 h to give 75% benzimidazole III. Hydrolysis of III gave a mixt. of 2 furanose isomers and a pyranose, the ratio of which depended on the solvent.

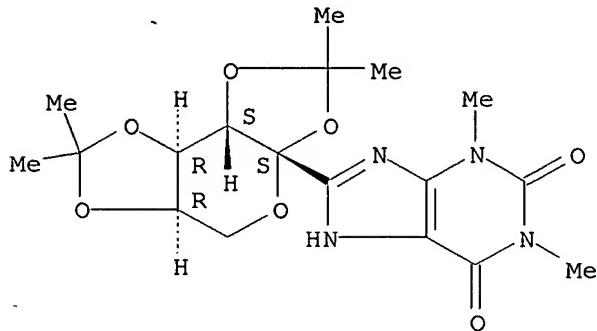
IT 76513-83-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of)

RN 76513-83-2 HCPLUS

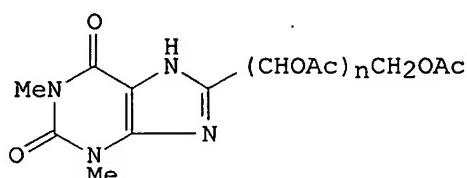
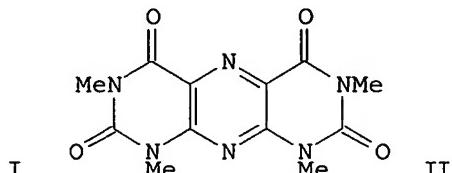
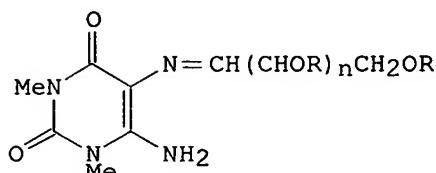
CN .beta.-D-Arabinopyranose, 1,2:3,4-bis-O-(1-methylethylidene)-1-C-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



1979:575651 Document No. 91:175651 Studies on heterocyclic compounds. XXV.  
 C-Glycosyl nucleoside. XI. Interaction of Schiff bases with metal halides in dimethyl sulfoxide. Sakaguchi, Masakazu; Miyata, Yoshihisa; Ogura, Haruo; Gonda, Kinji; Koga, Shozo; Okamoto, Toshihiko (Sch. Pharm. Sci., Kitasato Univ., Tokyo, 108, Japan). Chem. Pharm. Bull., 27(5), 1094-100 (English) 1979. CODEN: CPBTAL. ISSN: 0009-2363.

GI



III

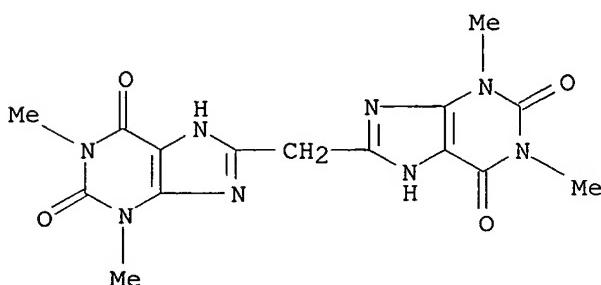
AB Reaction of Schiff bases I ( $R = H$ ,  $n = 3-4$ ), obtained from D-glucose, D-, and L-arabinose, with  $HgCl_2$  in  $Me_2SO$  at room temp. gave pyrimidopteridine II quant. I ( $R = Ac$ ,  $n = 3-4$ ) on similar reaction gave 37-40% nucleoside analogs III. Similar Schiff bases of 5,6-diamino-1,3-dimethyluracil and (.-+.)-glyceraldehyde or  $PhCHO$  gave the corresponding theophylline or pteridine derivs. while  $H_2NC(CN):C(CN)N:CHCH(OH)CH_2OH$  gave 2,3-dicyano-5-methylpyrazine.  $PdCl_2$  instead of  $HgCl_2$  gave the corresponding products, but in low yields.  $MgCl_2$ ,  $CaCl_2$ ,  $BaCl_2$ ,  $SrCl_2$ ,  $ZnCl_2$ , and  $CdCl_2$  gave no reaction with the Schiff bases.

IT 1784-51-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. of)

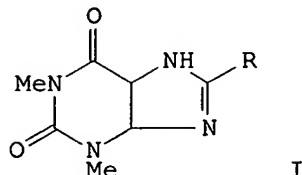
RN 1784-51-6 HCPLUS

CN 1H-Purine-2,6-dione, 8,8'-methylenebis[3,7-dihydro-1,3-dimethyl- (9CI)  
 (CA INDEX NAME)]

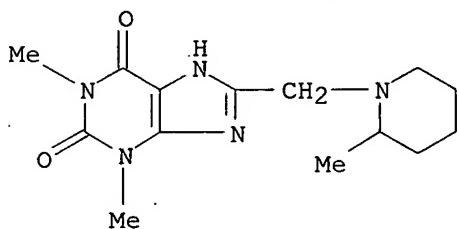


1979:575303 Document No. 91:175303 Synthesis of 8-theophyllineacetic acid, -propionic acid, and -methanamine derivatives. Kobor, Jeno; Szabo, Mrs. Matyas (Hung.). Juhasz Gyula Tanarkepzo Foiskola Tud. Kozl. (MASODIK RESZ), 31-40 (Hungarian) 1977. CODEN: JGTDKX.

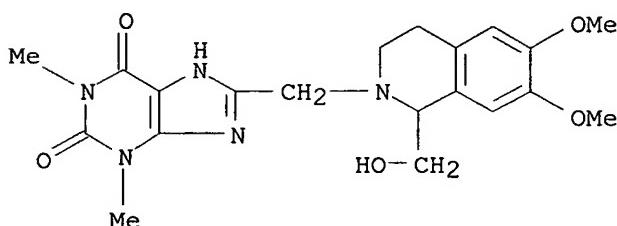
GI



- AB Theophyllines [I: R = CH<sub>2</sub>COOH, CH<sub>2</sub>COOEt, CH<sub>2</sub>CONHCH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>COOH, CH<sub>2</sub>CH<sub>2</sub>COC<sub>1</sub>, CH<sub>2</sub>C<sub>1</sub>, CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CONHCH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CONHCH<sub>2</sub>CH<sub>2</sub>OH, CH<sub>2</sub>CH<sub>2</sub>CONHCHEtCH<sub>2</sub>OH, CH<sub>2</sub>CH<sub>2</sub>CON(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>, morpholinocarbonylethyl, CH<sub>2</sub>CH<sub>2</sub>CONHCH<sub>2</sub>CH<sub>2</sub>C<sub>6</sub>H<sub>3</sub>-3,4-(OMe)<sub>2</sub>, CH<sub>2</sub>N(CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>OMe-4)<sub>2</sub>, CH<sub>2</sub>N(CHMe<sub>2</sub>)CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>, CH<sub>2</sub>N(CHMe<sub>2</sub>)CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, CH<sub>2</sub>NMeCH<sub>2</sub>CO<sub>2</sub>Et, 2-methylpiperidylmethyl, 1-hydroxymethyl-6,7-dimethoxy-1,2,3,4-tetrahydro-2-isouquinolinylmethyl] were prep'd. by Traube synthesis.
- IT 71798-30-6P 71798-31-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of)
- RN 71798-30-6 HCPLUS
- CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(2-methyl-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



- RN 71798-31-7 HCPLUS
- CN 1H-Purine-2,6-dione, 8-[[3,4-dihydro-1-(hydroxymethyl)-6,7-dimethoxy-2(1H)-isoquinolinyl]methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

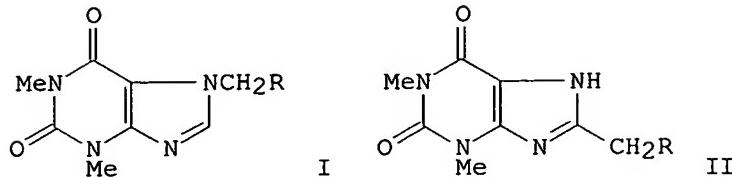


L5 ANSWER 125 OF 163 HCPLUS COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 1E01

1979:540815 Document No. 91:140815 Mannich bases of theophylline. Rida, S. M.; Farghaly, A. M.; Ashour, F. A. (Pharm. Chem. Dep., Fac. Pharm., Alexandria, Egypt). Pharmazie, 34(4), 214-16 (English) 1979. CODEN: PHARAT. ISSN: 0031-7144.

GI



AB The Mannich bases I (R = piperidino, 4-methylpiperazino, 4-(2-hydroxyethyl)piperazino, NEt<sub>2</sub>) were obtained in 80-91% yields by aminomethylating theophylline in EtOH with 38% CH<sub>2</sub>O at room temp. II was formed in 55-80% yield by treating theophylline with paraformaldehyde under reflux in EtOH for 20-30 h.

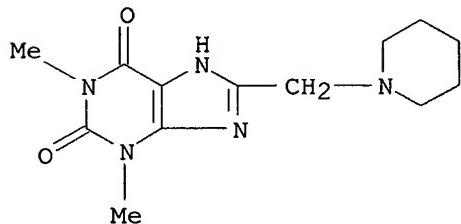
IT 5436-40-8P 65919-57-5P 71527-03-2P

71527-04-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

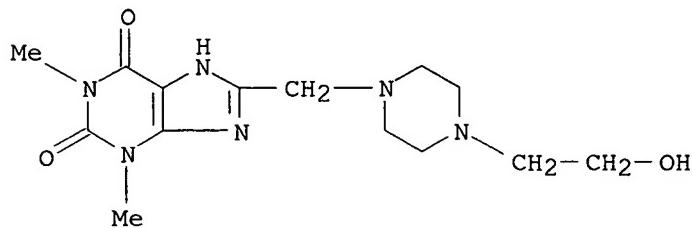
RN 5436-40-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinylmethyl)-(9CI) (CA INDEX NAME)



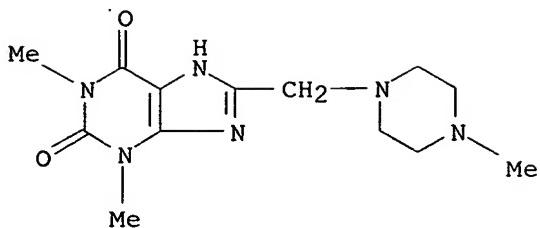
RN 65919-57-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(4-(2-hydroxyethyl)-1-piperazinyl)methyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



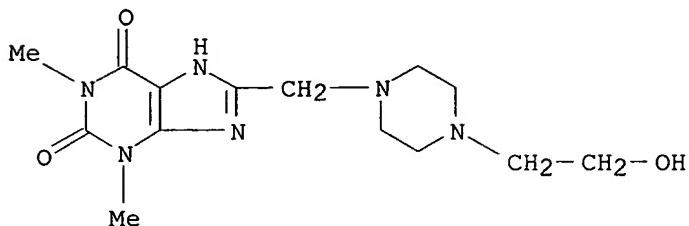
RN 71527-03-2 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



RN 71527-04-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[(4-(2-hydroxyethyl)-1-piperazinyl)methyl]-1,3-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

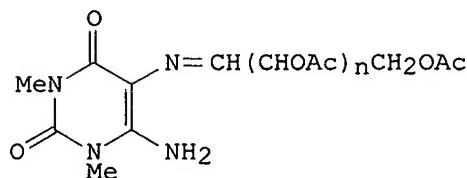


● 2 HCl

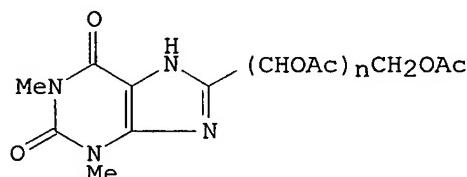
L5 ANSWER 126 OF 163 HCPLUS COPYRIGHT 2002 ACS

1979:439771 Document No. 91:39771 C-Glycosyl nucleosides. XVII. A novel reaction of Schiff bases with mercuric chloride in dimethyl sulfoxide. Ogura, Haruo; Sakaguchi, Masakazu; Okamoto, Toshihiko; Gonda, Kinji; Koga, Shozo (Sch. Pharm. Sci., Kitasato Univ., Tokyo, 108, Japan). Heterocycles, 12(3), 359-63 (English) 1979. CODEN: HTCYAM. ISSN: 0385-5414.

GI



I



II

AB Pteridine or theophylline derivs. were obtained from the reaction of

Searched by: Mary Hale 308-4258 CM-1 1E01

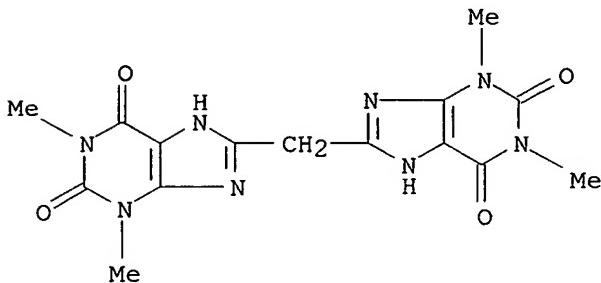
Schiff bases of 5,6-diamino-1,3-dimethyluracil with HgCl<sub>2</sub> in Me<sub>2</sub>SO via radical or ionic mechanisms, which were confirmed by time dependent ESR and NMR spectra. Reactions of Schiff bases of D-glucose, D-, and L-arabinose (I; n = 4 or 3) with HgCl<sub>2</sub> gave 35-40% theophylline nucleosides II.

IT 1784-51-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 1784-51-6 HCPLUS

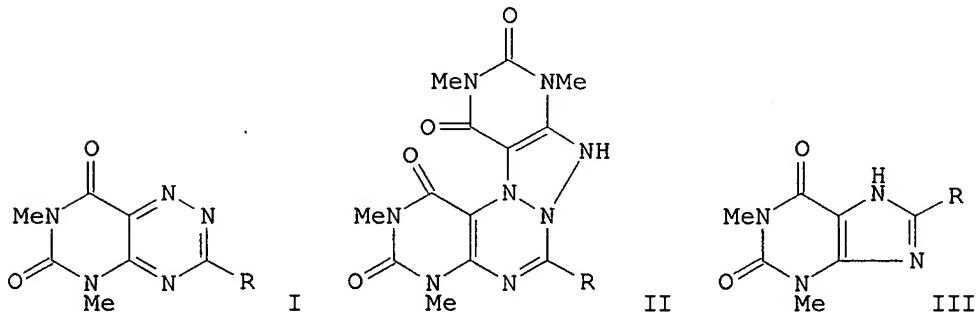
CN 1H-Purine-2,6-dione, 8,8'-methylenebis[3,7-dihydro-1,3-dimethyl- (9CI)  
(CA INDEX NAME)



L5 ANSWER 127 OF 163 HCPLUS COPYRIGHT 2002 ACS

1978:443346 Document No. 89:43346 Synthesis and properties of 1,3-dimethyl-6-azalumazines (isofervenulins). Yoneda, Fumio; Nagamatsu, Tomohisa; Ogiwara, Kazuko; Kanahori, Michiko; Nishigaki, Sadao; Taylor, Edward C. (Kumamoto Univ., Kumamoto, Japan). Chem. Pharm. Bull., 26(2), 367-73 (English) 1978. CODEN: CPBTAL. ISSN: 0009-2363.

GI



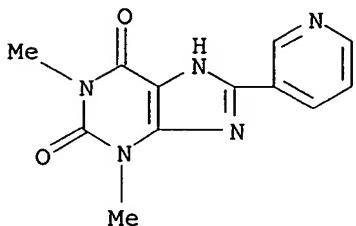
AB Cyclocondensation of 6-amino-1,3-dimethyl-5-nitrosouracil with RCONHNH<sub>2</sub> (R = H, Ph, 2-furyl, 2-thienyl, 3-pyridinyl, 4-pyridinyl) in refluxing DMF or sulfolane gave the isofervenulins I and azapurinoazapteridines II. II were also prep'd. by treatment of I with 6-amino-1,3-dimethyluracil in refluxing DMF. Treatment of I with Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> in hot HCO<sub>2</sub>H gave the theophyllines III.

IT 1029-62-5P 1088-64-8P 33797-74-9P

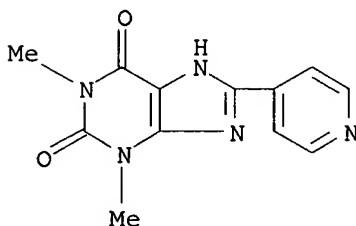
33797-75-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

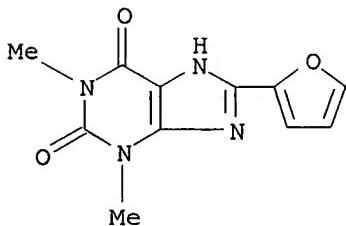
(prep. of, by ring contraction of azalumazine deriv.)  
RN 1029-62-5 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



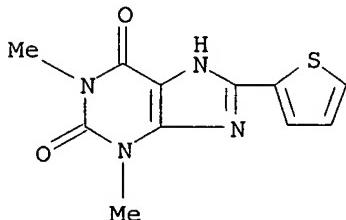
RN 1088-64-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



RN 33797-74-9 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



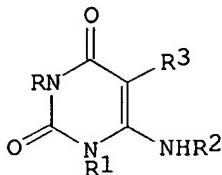
RN 33797-75-0 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



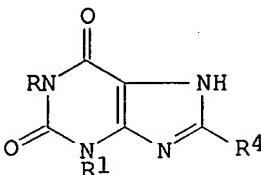
L5 ANSWER 128 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1978:190756 Document No. 88:190756 Purines, XII. Cyclization of 4-alkylamino-5-nitrosouracils and synthesis of 8-substituted xanthines and bis(theophyllin-8-yl)alkane derivatives. Fuchs, Herbert; Gottlieb, Margarete; Pfeiderer, Wolfgang (Fachber. Chem., Univ. Konstanz, Constance, Ger.). Chem. Ber., 111(3), 982-95 (German) 1978. CODEN: CHBEAM. ISSN: 0009-2940.

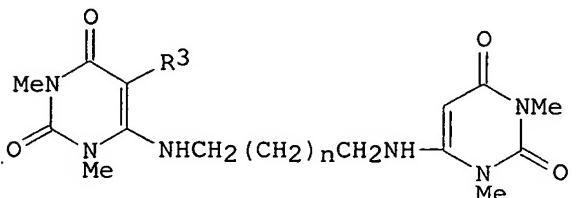
GI



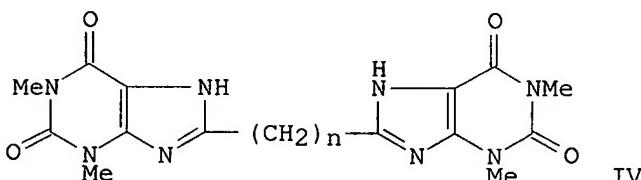
I



II



III



IV

AB Uracils I (R = Me, CHMe<sub>2</sub>, cyclohexyl, Ph; R1 = Et, Pr, Bu, CH<sub>2</sub>Ph, allyl, CHMe<sub>2</sub>, cyclohexyl, Ph; R2 = Me, CHMe<sub>2</sub>, CH<sub>2</sub>Ph, CH<sub>2</sub>CH<sub>2</sub>Ph, cyclohexyl, tetrahydrofuryl, R3 = H) were prepd. by chlorinating pyrimidinetrones followed by amination. I (R3 = NO) were obtained by nitrosating I (R3 = H) and in some cases were cyclized to xanthines II (R = R1 = Ph, R4 = H, Ph, CH<sub>2</sub>Ph, 2-tetrahydrofuryl; R = R1 = Me, R4 = 2-tetrahydrofuryl). Bis(uracyl)amines III (R3 = H, n = 0-8) were prepd. by treating 4-chloro-1,3-dimethyluracil with H<sub>2</sub>NCH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>CH<sub>2</sub>NH<sub>2</sub> and were nitrosated to give III (R3 = NO), which cyclized to IV.

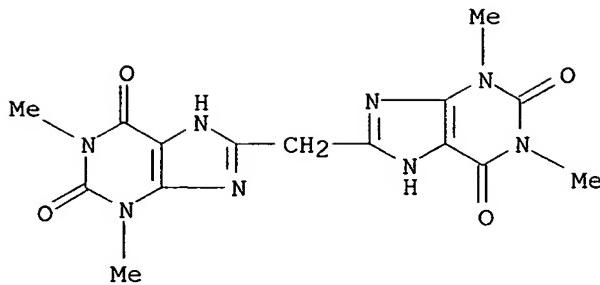
IT 1784-51-6P 1784-67-4P 34839-28-6P

66274-15-5P

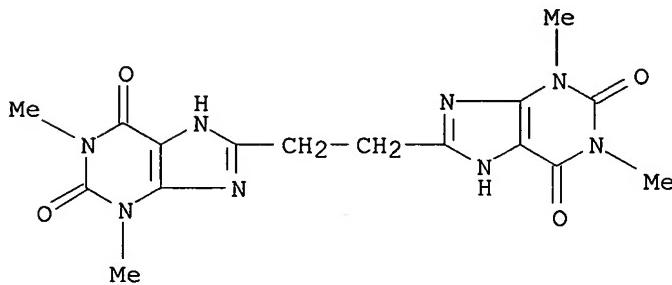
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 1784-51-6 HCAPLUS

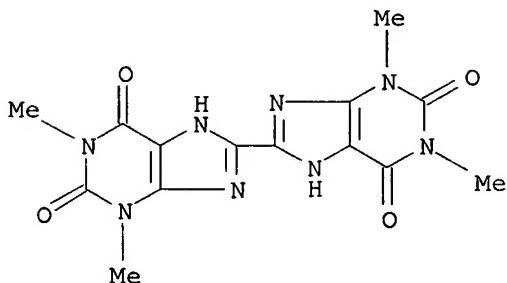
CN 1H-Purine-2,6-dione, 8,8'-methylenebis[3,7-dihydro-1,3-dimethyl- (9CI)  
(CA INDEX NAME)



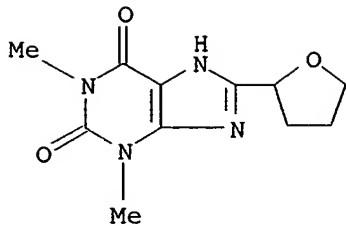
RN 1784-67-4 HCAPLUS  
 CN 1H-Purine-2,6-dione, 8,8'-(1,2-ethanediyl)bis[3,7-dihydro-1,3-dimethyl-  
 (9CI) (CA INDEX NAME)



RN 34839-28-6 HCAPLUS  
 CN [8,8'-Bi-1H-purine]-2,2',6,6'-tetrone, 3,3',7,7'-tetrahydro-1,1',3,3'-  
 tetramethyl- (9CI) (CA INDEX NAME)



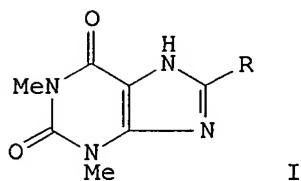
RN 66274-15-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2-furanyl)-  
 (9CI) (CA INDEX NAME)



L5 ANSWER 129 OF 163 HCPLUS COPYRIGHT 2002 ACS

1978:152567 Document No. 88:152567 Photochemistry of the purine system.  
Part II. Peroxide-initiated photoreactions of theophylline with ethers.  
Erndt, Aleksander; Para, Andrzej; Kostuch, Andrzej (Inst. Chem. Food  
Technol., Sch. Agric., Krakow, Pol.). Rocz. Chem., 51(12), 2421-5  
(English) 1977. CODEN: ROCHAC. ISSN: 0035-7677.

GI

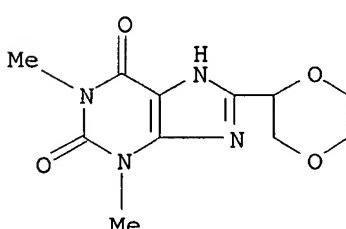


AB The title reactions were carried out 100-120 h under Ar using Q-400 high pressure Hg vapor immersion lamp to give I (R = 1,4-dioxan-2-yl, 2-tetrahydropyranyl, 2-tetrahydrofuryl, CHMeOEt, CHEtOPr, CMe<sub>2</sub>OCHMe<sub>2</sub>). A free-radical mechanism for the reaction was proved by the formation of the dehydrodimers of the ethers. UV, IR and NMR data are given.

IT 66274-13-3P 66274-14-4P 66274-15-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

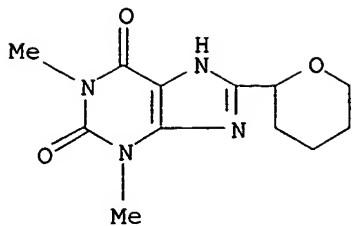
RN 66274-13-3 HCPLUS

CN 1H-Purine-2,6-dione, 8-(1,4-dioxan-2-yl)-3,7-dihydro-1,3-dimethyl- (9CI)  
(CA INDEX NAME)

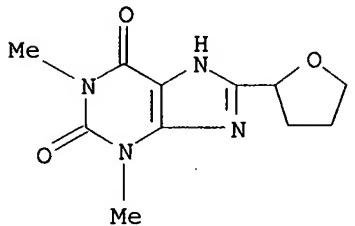


RN 66274-14-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2H-pyran-2-yl)-  
(9CI) (CA INDEX NAME)

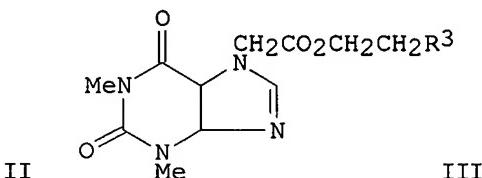
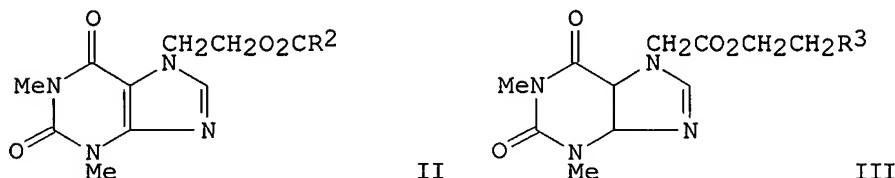
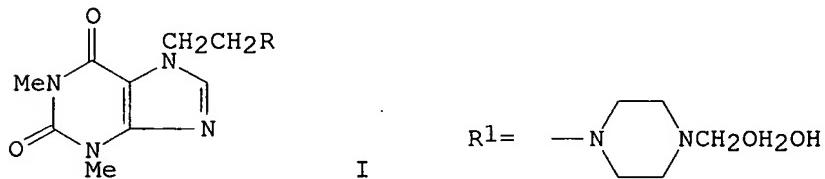


RN 66274-15-5 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(tetrahydro-2-furanyl)-  
 (9CI) (CA INDEX NAME)



L5 ANSWER 130 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1978:121110 Document No. 88:121110 Synthesis and pharmacological testing of some theophylline esters. Ride, S. M.; Farghaly, A. M.; Ashour, F. A. (Fac. Pharm., Alexandria Univ., Alexandria, Egypt). Pharmazie, 32(11), 672-6 (English) 1977. CODEN: PHARAT. ISSN: 0031-7144.

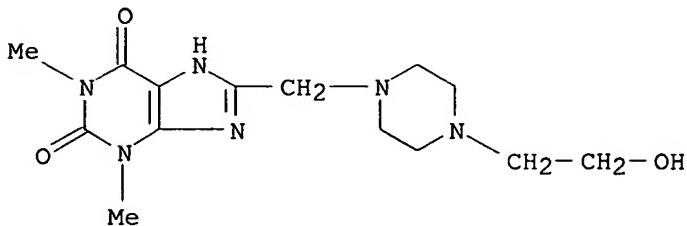
GI



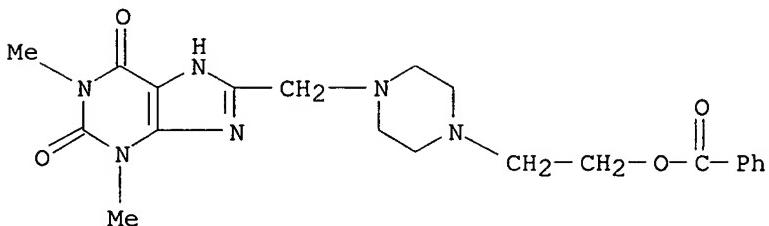
AB Theophylline derivs. I [R = OH, Cl, I, (HOCH2CH2)2N, (ClCH2CH2)2N, R1], II [R2 = PhCH2, PhCH:CH, Ph(AcO)CH, etc.] and III (R3 = Me2N, Et2N, piperidino, morpholino) (22 compds.) were prepd. for testing as atropine substitutes and spasmolytic activity.

IT 65919-57-5  
 RL: RCT (Reactant)

(acylation of, by benzoic acid)  
RN 65919-57-5 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



IT 65881-69-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 65881-69-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 8-[[4-[2-(benzoyloxy)ethyl]-1-piperazinyl]methyl]-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

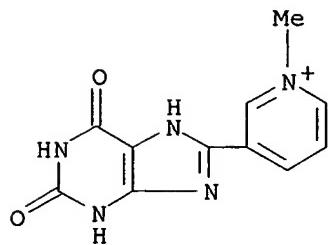


L5 ANSWER 131 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
1977:596313 Document No. 87:196313 Oxidation of hypoxanthines, bearing 8-aryl or 8-pyridyl substituents, by bovine milk xanthine oxidase.  
Bergmann, Felix; Levene, Lawrence; Govrin, Hanna (Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel). Biochim. Biophys. Acta, 484(2), 275-89 (English) 1977. CODEN: BBACAO.

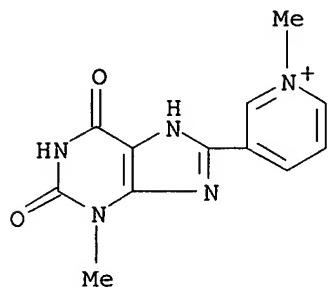
AB Hypoxanthines, contg. aryl or pyridyl substituents at position 8, were converted by bovine milk xanthine oxidase into their corresponding xanthines at low rates. Oxidn. was accelerated considerably when the 8-pyridyl substituents were quaternized. In the enzymic oxidn. of quaternary 8-pyridylhypoxanthines, a lag phase preceded the attainment of a const., max. reaction rate. The delay is assumed to be due to a relatively slow conformational change in the active enzymic center. In 8-(3'-N-methylpyridinio)xanthine betaine, the pyridinium moiety was also attacked at high pH (9-11) to yield an N-methyl-2-pyridone. The analogous pyridone was the only oxidn. product of 1-methyl-8-(3'-N-methylpyridinio)hypoxanthine betaine, which was not attacked in the pyrimidine ring. The cationic substrates were attracted to the enzyme by an anionic group, which probably formed an ion pair with a protonated NH<sub>2</sub> group in or near the active center.

IT 46891-31-0 46985-76-6 64709-31-5  
64709-36-0  
RL: PRP (Properties)  
(properties of)  
RN 46891-31-0 HCAPLUS

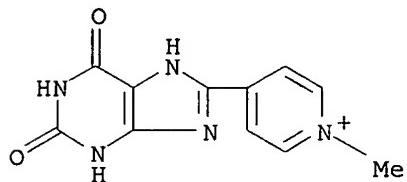
CN Pyridinium, 1-methyl-3-(2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl)- (9CI)  
(CA INDEX NAME)



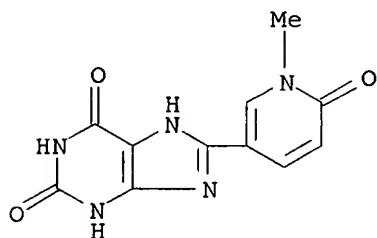
RN 46985-76-6 HCPLUS  
CN Pyridinium, 1-methyl-3-(2,3,6,7-tetrahydro-3-methyl-2,6-dioxo-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



RN 64709-31-5 HCPLUS  
CN Pyridinium, 1-methyl-4-(2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl)- (9CI)  
(CA INDEX NAME)



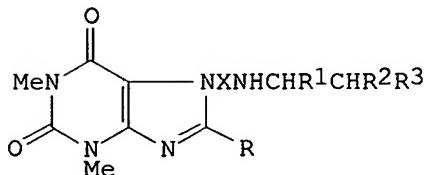
RN 64709-36-0 HCPLUS  
CN 1H-Purine-2,6-dione, 8-(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)-3,7-dihydro- (9CI) (CA INDEX NAME)



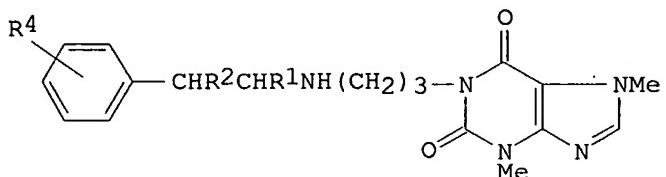
L5 ANSWER 132 OF 163 HCPLUS COPYRIGHT 2002 ACS

1977:423212 Document No. 87:23212 Synthesis of bronchospasmolytically effective .beta.-phenylethylaminoalkyl xanthines. Klingler, K. H. (Chem.-Synth. Abt., Chemiewerk Homburg, Frankfurt/Main, Ger.). Arzneim.-Forsch., 27(1A), 4-14 (German) 1977. CODEN: ARZNAD.

GI



I



II

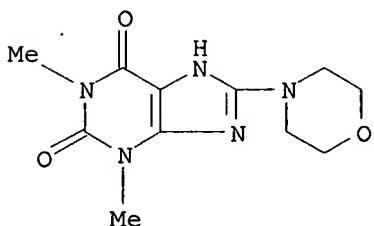
AB Xanthines I [X = (CH<sub>2</sub>)<sub>n</sub>, CH<sub>2</sub>CHMeCH<sub>2</sub>, CH<sub>2</sub>CHMe, CH<sub>2</sub>CH(OH)CH<sub>2</sub>; n = 2-4; R = H, morpholino, NEt<sub>2</sub>, NHCHMe<sub>2</sub>, NHCH<sub>2</sub>Ph, NHCH<sub>2</sub>CH<sub>2</sub>OH, 2-methylmorpholino, piperidino, Bu, CH<sub>2</sub>Ph, R<sub>1</sub> = Me, Et; R<sub>2</sub> = H, OH; R<sub>3</sub> = 4-HOC<sub>6</sub>H<sub>4</sub>, 3-HOC<sub>6</sub>H<sub>4</sub>, 3,4-(HO)C<sub>6</sub>H<sub>3</sub>, 3,4-Me(HO)C<sub>6</sub>H<sub>3</sub>, 3,5,4-Me<sub>2</sub>(HO)C<sub>6</sub>H<sub>2</sub>, 4,3,5-HO(Me<sub>3</sub>C)C<sub>6</sub>H<sub>2</sub>, 4,3,5-HO(Me<sub>2</sub>CH)C<sub>6</sub>H<sub>2</sub>, 3,5-(HO)C<sub>6</sub>H<sub>3</sub>, 2,5-(HO)C<sub>6</sub>H<sub>3</sub>, 4,3-HO(HOCH<sub>2</sub>)C<sub>6</sub>H<sub>3</sub>] and II (R<sub>1</sub> = Me, R<sub>2</sub> = H, R<sub>4</sub> = 4-OH; R<sub>1</sub> = H, R<sub>2</sub> = OH, R<sub>4</sub> = 3-OH) (90 compds.) were prep'd. by 8 std. methods.

IT 30958-49-7

RL: RCT (Reactant)  
(reaction of, with bromochloropropane)

RN 30958-49-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- (9CI)  
(CA INDEX NAME)

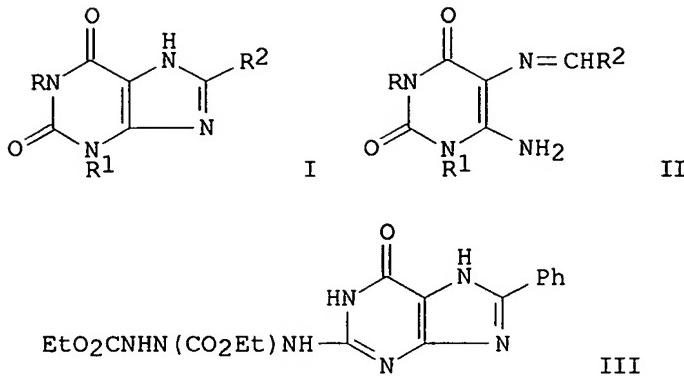


L5 ANSWER 133 OF 163 HCPLUS COPYRIGHT 2002 ACS

1977:89762 Document No. 86:89762 Dehydrogenative cyclization of 6-amino-5-benzylideneaminopyrimidines to purines with diethyl azodicarboxylate. Yoneda, Fumio; Higuchi, Masatsugu; Senya, Keitaro; Shimizu, Kayoko; Nishigaki, Sadao (Fac. Pharm. Sci., Kumamoto Univ.,

Kumamoto, Japan). Heterocycles, 4(11), 1759-64 (English) 1976. CODEN: HTCYAM.

GI



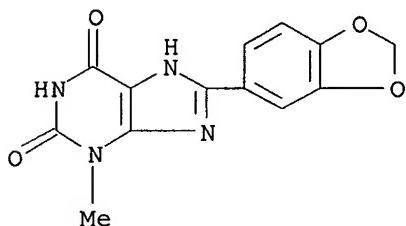
AB Fifteen purines I ( $R, R_1 = H, Me; R_2 = Ph, 4-ClC_6H_4, 3,4-Cl_2C_6H_3, 4-MeC_6H_4, 4-MeOC_6H_4, 4-Me_2NC_6H_4, 3,4-methylenedioxyphenyl$ ) were prepd. by dehydrogenative cyclization of the pyrimidines II in the presence of  $\text{EtO}_2\text{CN:NCO}_2\text{Et}$ . 5-Benzylidineamino-2,6-diamino-4-hydroxypyrimidine and  $\text{EtO}_2\text{CN:NCO}_2\text{Et}$  gave the purine III.

IT 61885-28-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 61885-28-7 HCAPLUS

CN 1H-Purine-2,6-dione, 8-(1,3-benzodioxol-5-yl)-3,7-dihydro-3-methyl- (9CI)  
(CA INDEX NAME)



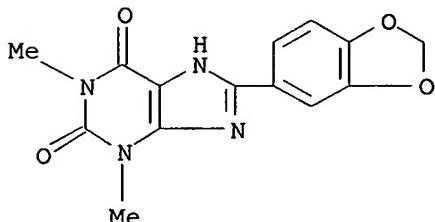
L5 ANSWER 134 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1975:410001 Document No. 83:10001 New synthesis of purines by the reaction of diethyl azodicarboxylate with 6-(alkylamino)uracils. Yoneda, Fumio; Matsumoto, Shigeru; Higuchi, Masastugu (Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, Japan). J. Chem. Soc., Chem. Commun. (5), 146-7 (English) 1975. CODEN: JCCCAT.

GI For diagram(s), see printed CA Issue.

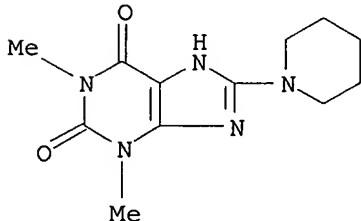
AB 6-(Alkylamino)uracils I ( $R = R_1 = Me, R_2 = Et, Pr, Ph; R = Me, R_1 = H, R_2 = Ph; R = H, R_1 = Me, R_2 = Ph$ ) reacted with 3 equiv.  $\text{EtO}_2\text{CN:NCO}_2\text{Et}$  to give 30-83% of the corresponding xanthine derivs. II. Treatment of the uracil III with aryl aldehydes gave the corresponding xanthine derivs. Thus,  $\text{PhCHO}$  with III at 170.degree. for 4 hr gave 72% corresponding xanthine deriv. II ( $R = R_1 = Me, R_2 = Ph$ ).

IT **20886-69-5P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. of)  
 RN 20886-69-5 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-(1,3-benzodioxol-5-yl)-3,7-dihydro-1,3-dimethyl-  
 (9CI) (CA INDEX NAME)



L5 ANSWER 135 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1975:170185 Document No. 82:170185 Search for new drugs in the group of  
 xanthine derivatives. XXXVIII. 1,3-Dimethyl-8-alkyl-6H,7H,10H-(1,2,4)-  
 triazepine[4,3-f]purine-2,4-(1H,3H)-diones and their derivatives.  
 Eckstein, M.; Zajaczkowska, J. (Dep. Chem. Technol. Drugs, Med. Acad.,  
 Krakow, Pol.). Farmaco, Ed. Sci., 30(2), 122-7 (English) 1975. CODEN:  
 FRPSAX.

GI For diagram(s), see printed CA Issue.  
 AB Cyclization of 1-(8-chlorotheophyllin-7-yl)-3-butanone and -3-pentanone  
 with H2NNH2 gave the triazepinopurinedione I (R = Me, Et, R1 = H), which  
 were acylated to give I (R1 = MeCO, EtCO) and treated with CH2:CHCN to  
 give I (R1 = CH2CH2CN). Reaction of the ketones with substituted  
 hydrazines gave only hydrazone.  
 IT **961-48-8P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. of)  
 RN 961-48-8 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinyl)- (9CI)  
 (CA INDEX NAME)



L5 ANSWER 136 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1975:97986 Document No. 82:97986 A uracil-imidazolidinone rearrangement.  
 Klemm, Kurt; Pruesse, Wolfgang (Forschungslab., Byk Gulden-Pharma-Gruppe,  
 Constance, Ger.). Justus Liebigs Ann. Chem., Volume Date 1974 (11),  
 1882-9 (German) 1975. CODEN: JLACBF.  
 GI For diagram(s), see printed CA Issue.  
 AB Alkali treatment of the aminonitrosouracils I [R = NHR1, R1 =  
 (4-phenyl-1-piperazinyl)propyl, H, (CH2)3OH, or Et] led under ring  
 cleavage at C-6 to the diimino-imidazolidinones II. Under the same

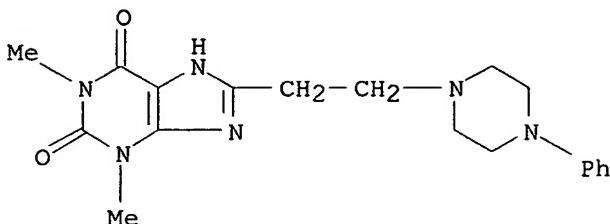
conditions, I ( $R = OH$ ) was cleaved preferentially at C-2 to give  $(MeNHCO)2C:NOH$ .

IT 54819-37-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 54819-37-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 137 OF 163 HCPLUS COPYRIGHT 2002 ACS

1975:80351 Document No. 82:80351 Piperazine derivatives of methylxanthines.

I. Chemical and pharmacological properties of 8-piperazinotheophyllines.  
Gorczyca, M.; Zejc, A.; Krupinska, J.; Czarnecki, R. (Dep. Pharm. Chem.,  
Med. Acad. Cracow, Krakow, Pol.). Farmaco, Ed. Sci., 29(10), 802-10  
(English) 1974. CODEN: FRPSAX.

GI For diagram(s), see printed CA Issue.

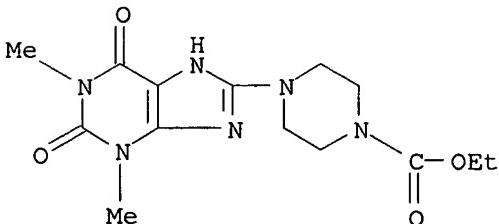
AB 8-Bromotheophylline [10357-68-3] was heated with the appropriate  
piperazines to yield 8-piperazinotheophylline (I) [54119-57-2],  
N-(8-theophyllinyl)-N'-methylpiperazine [52943-65-4],  
N-(8-theophyllinyl)-N'-beta.-hydroxyethylpiperazine [40171-75-3]  
, and N-(8-theophyllinyl)-N'-benzylpiperazine [54119-58-3]. I  
had a strong antihistaminic action on guinea pig trachea and a weak one on  
guinea pig and rat ileum. Tests on exptl. animals showed that the acute  
toxicities of these compds. were lower than those of aminophylline  
[317-34-0] and theophylline Na acetate [8002-89-9], and their hypotensive  
and cardiac actions were weaker than those of aminophylline.

IT 54119-63-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and hydrolysis of)

RN 54119-63-0 HCPLUS

CN 1-Piperazinecarboxylic acid, 4-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-  
1H-purin-8-yl)-, ethyl ester (9CI) (CA INDEX NAME)



IT 40171-75-3P 52943-65-4P 54119-57-2P

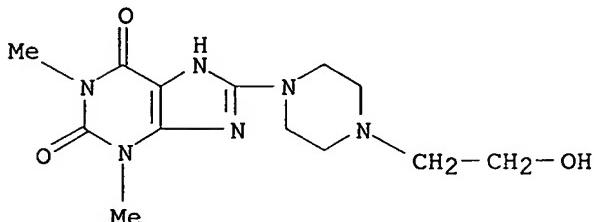
54119-58-3P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological  
process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(prep. and pharmacol. of)

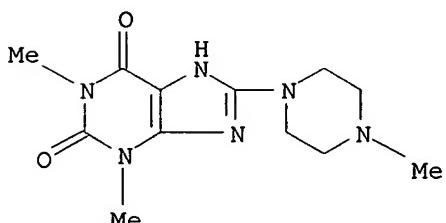
RN 40171-75-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[4-(2-hydroxyethyl)-1-piperazinyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



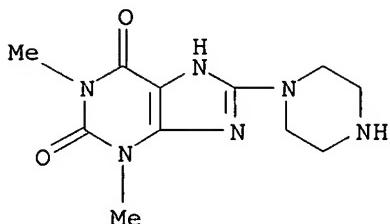
RN 52943-65-4 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



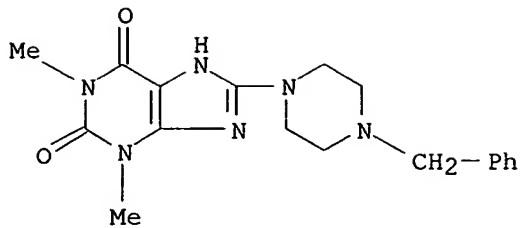
RN 54119-57-2 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 54119-58-3 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[4-(phenylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



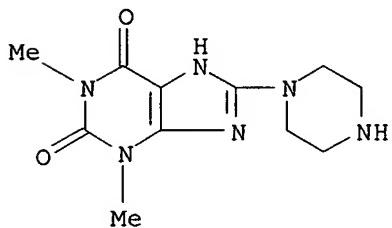
IT 54119-59-4P 54119-60-7P 54119-61-8P

54119-62-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 54119-59-4 HCAPLUS

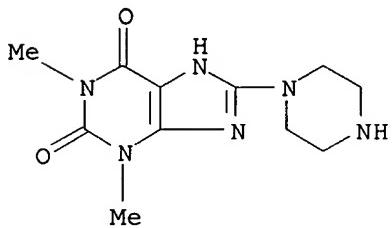
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperazinyl)-,  
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 54119-60-7 HCAPLUS

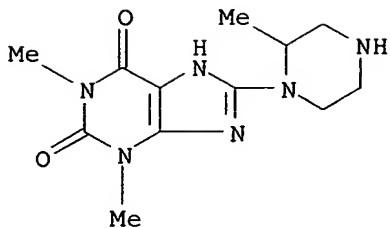
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperazinyl)-,  
monohydrobromide (9CI) (CA INDEX NAME)



● HBr

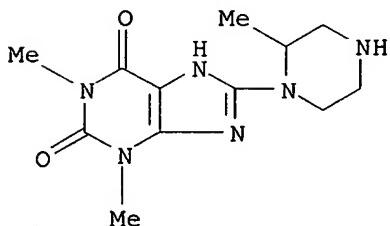
RN 54119-61-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



RN 54119-62-9 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-methyl-1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L5 ANSWER 138 OF 163 HCPLUS COPYRIGHT 2002 ACS

1975:31305 Document No. 82:31305 Syntheses of substituted 8-aminopurine derivatives. Yoneda, Fumio; Higuchi, Masatsugu (Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, Japan). Chem. Pharm. Bull., 22(7), 1658-60 (English) 1974. CODEN: CPBTAL.

GI For diagram(s), see printed CA Issue.

AB 6-Amino-1,3-dimethyl-5-nitrosouracil was treated with p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl to give the theophylline I (R = MeNH). I (R = NO<sub>2</sub>) was treated with p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl in pyridine to give the betaine II.

IT 54254-49-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 54254-49-8 HCPLUS

L5 ANSWER 139 OF 163 HCPLUS COPYRIGHT 2002 ACS

1974:437537 Document No. 81:37537 Substitution derivatives of theophylline at the 7 and 8 positions. Lespagnol, Albert; Van Aerde, Christine (Lab. Pharm. Chim., Fac. Pharm., Lille, Fr.). C. R. Acad. Sci., Ser. C, 278(18), 1145-7 (French) 1974. CODEN: CHDCAQ.

GI For diagram(s), see printed CA Issue.

AB Theophyllines I [R = H, CH<sub>2</sub>CO<sub>2</sub>Et; R<sub>1</sub> = [(3-phenoxyazin-5-ylpropyl)amino], N-methylpiperazino, PhOCH<sub>2</sub>CH<sub>2</sub>NH, Ph<sub>2</sub>CHNH, (PhCH<sub>2</sub>)<sub>2</sub>N, PhCH<sub>2</sub>(PhCH<sub>2</sub>CH<sub>2</sub>)N] were prepd. by treating I (R<sub>1</sub> = Br) with the amine. Reaction of I (R = CH<sub>2</sub>CO<sub>2</sub>Et, R<sub>1</sub> = Br) with H<sub>2</sub>NCHPh<sub>2</sub> also gave I (R = CH<sub>2</sub>CONHCHPh<sub>2</sub>, R<sub>1</sub> = NHCHPh<sub>2</sub>). The reaction of I (R = H, R<sub>1</sub> = Br) with pyridine gave the ylide II and hydrated derivs., both isolable. The phenoxyazinylpropylamines III (R<sub>2</sub> = H, Cl, CF<sub>3</sub>, OMe; R<sub>3</sub> = (CH<sub>2</sub>)<sub>3</sub>NH<sub>2</sub>) were prepd. by cyanoethylating III (R<sub>3</sub> = H) and reducing the resulting III (R<sub>3</sub> = CH<sub>2</sub>CH<sub>2</sub>CN).

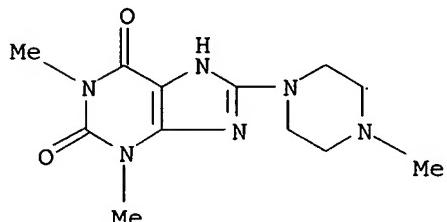
IT 52943-65-4P 52943-66-5P 52943-67-6P

**52943-89-2P 52986-19-3P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

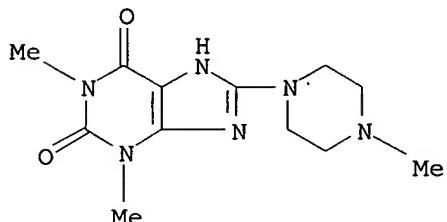
RN 52943-65-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



RN 52943-66-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-methyl-1-piperazinyl)-,  
hydrochloride (9CI) (CA INDEX NAME)



●x HCl

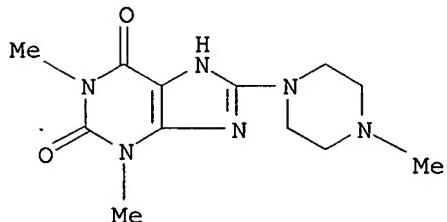
RN 52943-67-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-methyl-1-piperazinyl)-,  
compd. with iodomethane (9CI) (CA INDEX NAME)

CM 1

CRN 52943-65-4

CMF C12 H18 N6 O2

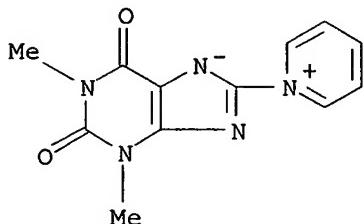


CM 2

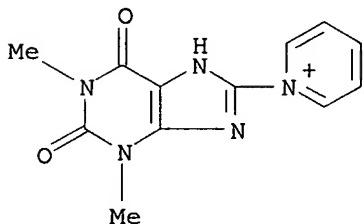
CRN 74-88-4  
CMF C H3 I

H<sub>3</sub>C-I

RN 52943-89-2 HCPLUS  
CN Pyridinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, inner salt (9CI) (CA INDEX NAME)



RN 52986-19-3 HCPLUS  
CN Pyridinium, 1-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, hydroxide (9CI) (CA INDEX NAME)



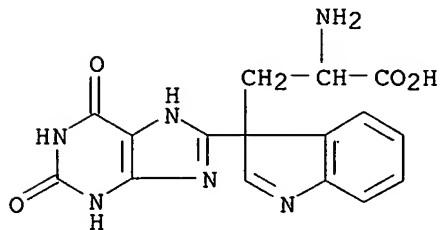
● OH<sup>-</sup>

L5 ANSWER 140 OF 163 HCPLUS COPYRIGHT 2002 ACS  
1974:422067 Document No. 81:22067 Purine N-oxides. 54. Chemical adduct of tryptophan and the oncogen 3-acetoxyxanthine. Stoehr, Gerhard; Salemnick, Gad; Brown, George Bosworth (Mem. Sloan-Kettering Cancer Cent., New York, N. Y., USA). Biochemistry, 12(25), 5084-6 (English) 1973.  
CODEN: BICHAW.

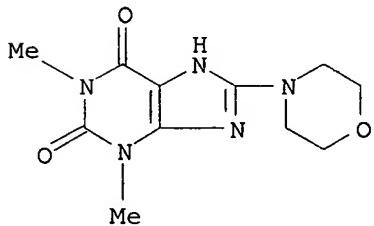
AB Two products of the reaction of L-tryptophan [73-22-3] and the oncogen 3-acetoxyxanthine [22052-01-3] at neutral pH are the diastereoisomeric [3-(2-amino-2-carboxyethyl)-3-(8-xanthinyl)]indolenine (I). These isomers can be isolated together in a 25% yield. A portion of the tryptophan was simultaneously oxidized to unidentified colored products, and approx. 30% was recovered unchanged. A metabolic expt. with 8-14C-labeled 3-hydroxyxanthine in the rat indicated that 0.25% of the total urinary radioactivity accompanied one of the I isomers in 3 sequential chromatog. systems.

IT 52046-79-4P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

RN 52046-79-4 HCAPLUS  
CN 3H-Indole-3-propanoic acid, .alpha.-amino-3-(2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl)- (9CI) (CA INDEX NAME)



L5 ANSWER 141 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
1973:466386 Document No. 79:66386 8-Substituted xanthine derivatives.  
Klingler, Karl H. (Deutsche Gold- und Silber-Scheideanstalt vorm.  
Roessler). Ger. Offen. DE 2253075 19730524, 28 pp. (German). CODEN:  
GWXXBX. APPLICATION: DE 1972-2253075 19721028.  
GI For diagram(s), see printed CA Issue.  
AB Thirteen title compds. [I; Rn = 3,4-(HO)2, 4-HO, 3,5-(HO)2, 3,4-Me(HO), or  
3,5,4-Me2(HO); R1 = NEt2, morpholino, CH2Ph, Bu, piperidino, or  
2-methylmorpholino; R2 = H or Me], useful as broncholytic or circulatory  
drugs, were prep'd. mainly as hydrochlorides either by reaction of  
(optionally N-benzyl-protected) amino derivs. II with YCHR1COC6H5-nRn (Y  
= Cl or Br) and subsequent catalytic hydrogenation or alternately of II  
with BrCHR2CH(OH)C6H5-nRn.  
IT 30958-49-7  
RL: RCT (Reactant)  
(reaction with chlorobromopropane)  
RN 30958-49-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- (9CI)  
(CA INDEX NAME)



L5 ANSWER 142 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
1973:466323 Document No. 79:66323 Thio analogs of 6-substituted  
1,3-dimethyl-7-azalumazine (fervenulin) and 7-substituted  
1,3-dimethyl-6-azalumazine (isofervenulin). Yoneda, Fumio; Sakuma,  
Yoshiharu; Ueno, Michiko; Nishigaki, Sadao (Fac. Pharm. Sci., Kumamoto  
Univ., Kumamoto, Japan). Chem. Pharm. Bull., 21(5), 926-30 (English)  
1973. CODEN: CPBTAL.  
GI For diagram(s), see printed CA Issue.  
AB 1,3-Dimethyl-4-thioxo-7-azalumazine derivs. (5-thiofervenulins) (I) and  
1,3-dimethyl-4-thioxo-6-azalumazine derivs. (5-thioisofervenulins) (II)  
were synthesized by the thiation of 1,3-dimethyl-7-azalumazine derivs.

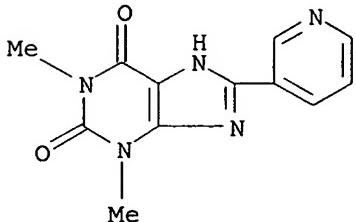
(fervenulins) and 1,3-dimethyl-6-azalumazine derivs. (isofervenulins). II were converted into theophyllines by treatment with sodium dithionite in HCO<sub>2</sub>H.

IT 1029-62-5P 1088-64-8P 33797-75-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepns. of)

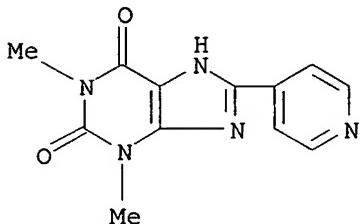
RN 1029-62-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



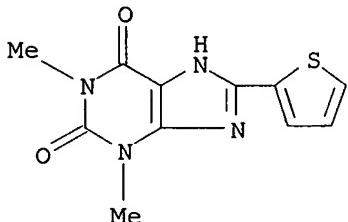
RN 1088-64-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



RN 33797-75-0 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 143 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1973:124636 Document No. 78:124636 Pharmacologically active  
8-aminotheophylline derivatives. Laboratoire Lebrun S. A. (Laboratoire le  
Brun S. A.). Fr. Demande FR 2132582 19721229, 17 pp. (French). CODEN:  
FRXXBL. APPLICATION: FR 1971-12761 19710409.

GI For diagram(s), see printed CA Issue.

AB The aminothiotheophyllines [I; X = S; R, R1 = alkyl, alkoxyalkyl,  
hydroxyalkyl, aralkyl (92 compds.)], useful as spasmolytics, coronary

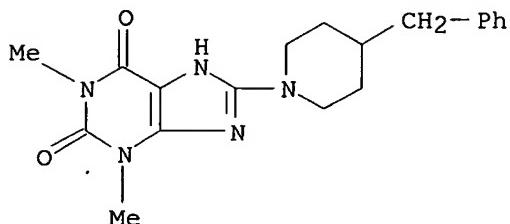
dilators, antihitaminics, parasympatholytics, or antitussives, were prep'd. by treating the corresponding theophylline (I, X = O) with P2S5. Thus, I (X = S, R = R1 = Et) was refluxed with P2S5 in dry pyridine to give 90% I (X = S, R = R1 = Et).

IT 40171-78-6

RL: RCT (Reactant)  
(reaction with phosphorus pentasulfide)

RN 40171-78-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-(phenylmethyl)-1-piperidinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 144 OF 163 HCPLUS COPYRIGHT 2002 ACS

1973:124541 Document No. 78:124541 Reactions of 8-(3-pyridyl)-6-thioxanthines with methyl iodide. Kleiner, Mordechai (Dep. Pharmacol., Heb. Univ., Jerusalem, Israel). J. Chem. Soc., Perkin Trans. 1 (7), 739-43 (English) 1973. CODEN: JCPRB4.

GI For diagram(s), see printed CA Issue.

AB 8-(3-Pyridyl)-6-thioxanthine with MeI in DMF gave the corresponding 6-thio ether which with an excess of MeI reacted furthur resulting in the quaternization of the pyridine N atom, methylation of N-1 and N-3, and de-S-methylation to give the N-methylthioxanthine derivs. (I, R = H and Me).

IT 1029-62-5P 15846-81-8P 40312-71-8P

40312-72-9P 40312-73-0P 40312-74-1P

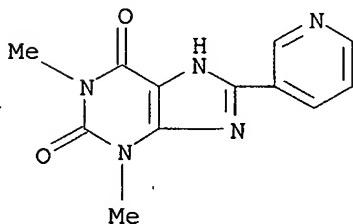
40312-79-6P 40487-79-4P 40864-52-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

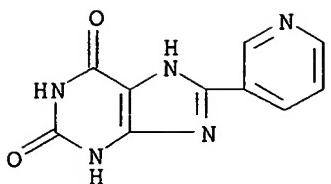
RN 1029-62-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



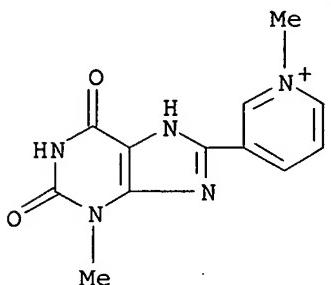
RN 15846-81-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 40312-71-8 HCAPLUS

CN Pyridinium, 1-methyl-3-(2,3,6,7-tetrahydro-3-methyl-2,6-dioxo-1H-purin-8-yl)-, hydroxide (9CI) (CA INDEX NAME)



● OH<sup>-</sup>

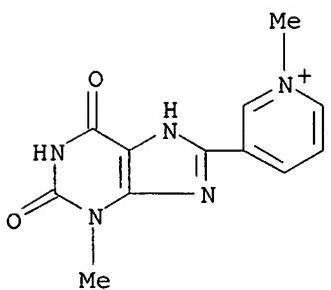
RN 40312-72-9 HCAPLUS

CN Pyridinium, 1-methyl-3-(2,3,6,7-tetrahydro-3-methyl-2,6-dioxo-1H-purin-8-yl)-, salt with 2,4,6-trinitrophenol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 46985-76-6

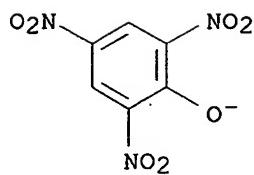
CMF C12 H12 N5 O2



CM 2

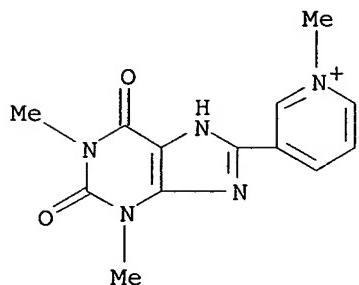
CRN 14798-26-6

CMF C6 H2 N3 O7



RN 40312-73-0 HCAPLUS

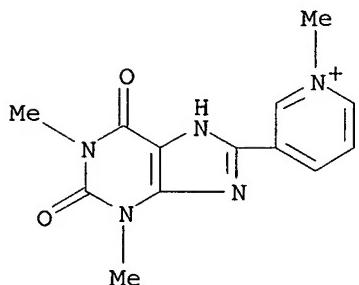
CN Pyridinium, 1-methyl-3-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, hydroxide (9CI) (CA INDEX NAME)



●  $\text{OH}^-$

RN 40312-74-1 HCAPLUS

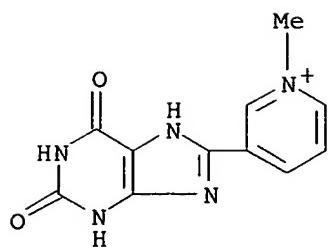
CN Pyridinium, 1-methyl-3-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, iodide (9CI) (CA INDEX NAME)



●  $\text{I}^-$

RN 40312-79-6 HCAPLUS

CN Pyridinium, 1-methyl-3-(2,3,6,7-tetrahydro-2,6-dioxo-1H-purin-8-yl)-, hydroxide (9CI) (CA INDEX NAME)



● OH<sup>-</sup>

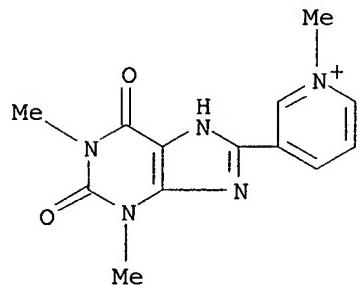
RN 40487-79-4 HCPLUS

CN Pyridinium, 1-methyl-3-(2,3,6,7-tetrahydro-1,3-dimethyl-2,6-dioxo-1H-purin-8-yl)-, salt with 2,4,6-trinitrophenol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 47070-96-2

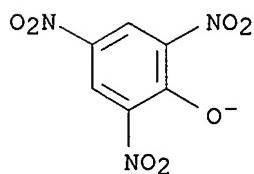
CMF C13 H14 N5 O2



CM 2

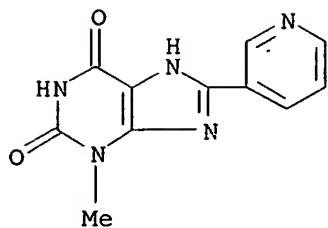
CRN 14798-26-6

CMF C6 H2 N3 O7



RN 40864-52-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3-methyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 145 OF 163 HCPLUS COPYRIGHT 2002 ACS

1973:72181 Document No. 78:72181 8-Aminothephylline derivatives.

(Laboratoire Lebrun S. A.). Fr. Demande FR 2116302 19720818, 15 pp.  
(French). CODEN: FRXXBL. APPLICATION: FR 1970-43891 19701207.

GI For diagram(s), see printed CA Issue.

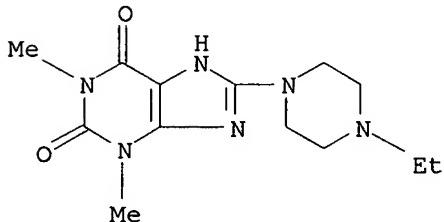
AB 8-Aminothephyllines I (R = alkyl, aralkyl, hydroxyalkyl, chloroalkyl, aminoalkyl; R1 = alkyl, aralkyl, aminoalkyl; NRR1 = substituted piperazino, piperidino, pyrrolidino) (52 compds.) were prep'd. by treating 8-chlorothephylline or 8-bromothephylline with RR1NH. I displayed coronary dilator, diuretic, spasmolytic, and bronchodilator activities greater than that of theophylline, accompanied by lower toxicity.

IT 40171-74-2P 40171-75-3P 40171-76-4P  
40171-77-5P 40171-78-6P 40171-79-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of)

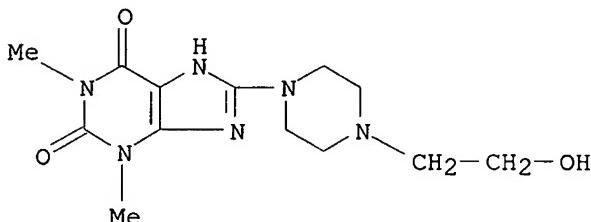
RN 40171-74-2 HCPLUS

CN 1H-Purine-2,6-dione, 8-(4-ethyl-1-piperazinyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



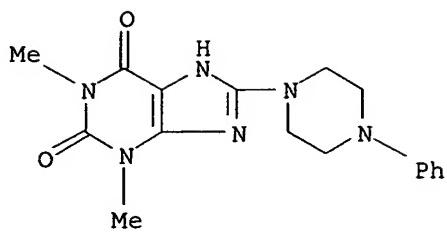
RN 40171-75-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[4-(2-hydroxyethyl)-1-piperazinyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



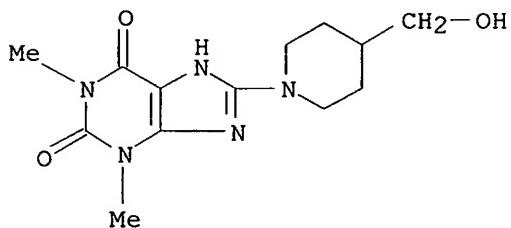
RN 40171-76-4 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-phenyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



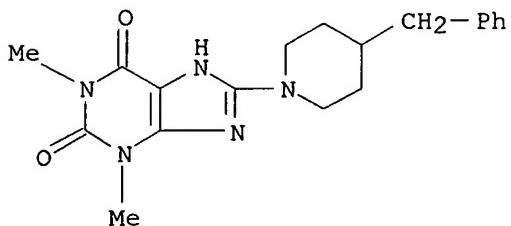
RN 40171-77-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[4-(hydroxymethyl)-1-piperidinyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



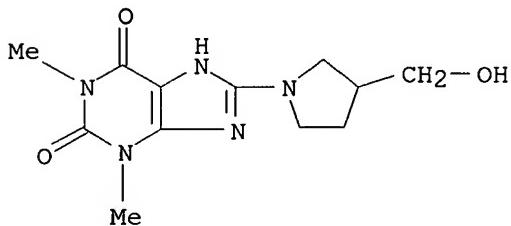
RN 40171-78-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-[4-(phenylmethyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 40171-79-7 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-[3-(hydroxymethyl)-1-pyrrolidinyl]-1,3-dimethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 146 OF 163 HCPLUS COPYRIGHT 2002 ACS

1972:58647 Document No. 76:58647 Electrochemical oxidation of theophylline

Searched by: Mary Hale 308-4258 CM-1 1E01

at the pyrolytic graphite electrode. Hansen, Barbara H.; Dryhurst, Glenn (Dep. Chem., Univ. Oklahoma, Norman, Okla., USA). J. Electroanal. Chem. Interfacial Electrochem., 32(3), 405-14 (English) 1971. CODEN: JEIEBC.

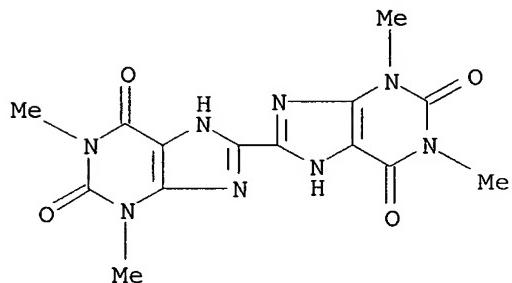
GI For diagram(s), see printed CA Issue.

AB During the electrochem. oxidn. of theophylline at the title electrode, the primary electron transfer process occurred by a 1-electron, 1-proton oxidn. of the C-8:N-9 bond to give a free radical species, which partly dimerized to give a previously unreported compd., 8-(1,3-dimethylxanth-8-yl)-1,3-dimethylxanthine (I). Part of the free radical was oxidized in a 1-electron, 1-proton reaction to give 1,3-dimethyluric acid, which was further oxidized in a 2-electron, 2-proton reaction at the C-4:C-5 bond to give 1,3-dimethyluric acid-4,5 diol. The latter unstable species underwent a secondary electrochem oxidn. to parabanic acid and dimethylurea, and fragmentation to dimethylalloxan and urea and 6,8-dimethylallantoin and CO<sub>2</sub>. The oxidn. was studied by voltammetry and controlled potential electrolysis.

IT 34839-28-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. of)

RN 34839-28-6 HCPLUS

CN [8,8'-Bi-1H-purine]-2,2',6,6'-tetrone, 3,3',7,7'-tetrahydro-1,1',3,3'-tetramethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 147 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1971:529766 Document No. 75:129766 Synthesis and properties of 1,3-dimethyl-6-azalumazines. Yoneda, Fumio; Ogiwara, Kazuko; Kanahori, Michiko; Nishigaki, Sadao (Sch. Med., Keio Univ., Tokyo, Japan). Chem. Biol. Pteridines, Proc. Int. Symp., 4th, Meeting Date 1969, 145-53. Editor(s): Iwai, K. Int. Acad. Print. Co.: Tokyo, Japan. (English) 1970. CODEN: 23BVAJ.

GI For diagram(s), see printed CA Issue.

AB Heating 6-amino-5-nitrosouracil (I) with a stoichiometric amt. of HCONHNH<sub>2</sub> in aprotic solvents such as DMF, Me<sub>2</sub>SO or sulfolane yielded about 15% II (R = H), m. 199-200.degree.. When Me<sub>2</sub>SO or sulfolane was used as the solvent, the main product was 1,3,6,8-tetramethyl-2,4,5,7(1H,3H,6H,8H)-pyrimido[5,4-g]pteridinetetrone (IIa). Similarly prep'd. were II (R and % yield given): Ph, 26.0; 2-furyl (III), 21.3; 2-thienyl, 23.3; nicotinyl (IV), 35.9; isonicotinyl, 27.4. Several common patterns in the mass spectra of II permitted some generalization about the mechanism of fragmentation. II treated with Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> in HCO<sub>2</sub>H gave .delta.-substituted theophyllines (V) by reductive ring contraction. III and IV exhibited antibacterial activity against Escherichia coli at 25 and 100 .mu.g/ml, resp. IV inhibited plaque formation in Newcastle disease virus at 0.5 mg/ml in the agar diffusion test and no cytotoxic effect was observed at 16 mg/ml.

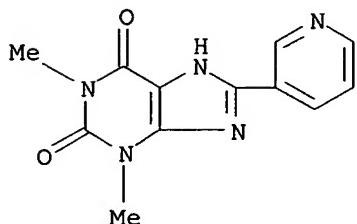
IT 1029-62-5P 1088-64-8P 33797-74-9P

**33797-75-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep. of)

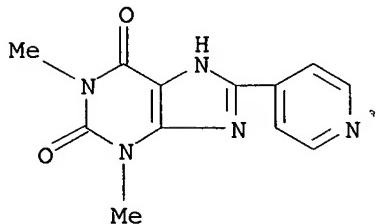
RN 1029-62-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA  
INDEX NAME)



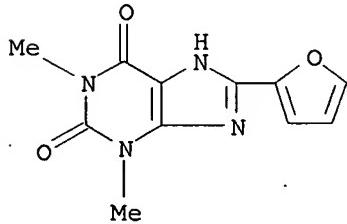
RN 1088-64-8 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA  
INDEX NAME)



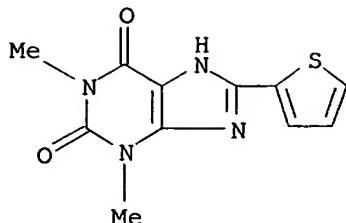
RN 33797-74-9 HCPLUS

CN 1H-Purine-2,6-dione, 8-(2-furanyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA  
INDEX NAME)

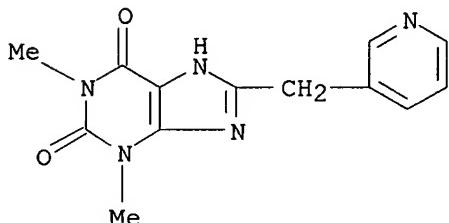


RN 33797-75-0 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-thienyl)- (9CI) (CA  
INDEX NAME)

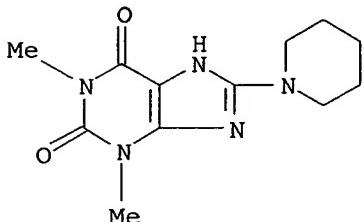


- L5 ANSWER 148 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
 1971:141706 Document No. 74:141706 8-(3-Pyridylmethyl)theophylline derivatives. Lespagnol, Albert; Debaert, Michel; Minard-Vaillant, Nicole (Lab. Pharm. Chim., U.E.R. Pharm., Lille, Fr.). Chim. Ther., 5(5), 321-6 (French) 1970. CODEN: CHTPBA.
- AB The starting material 1,3-dimethyl-4,5-diaminouracil (I) required for the synthesis of 8-(3-pyridylmethyl)theophylline (II) was prepd. preferentially by condensation of (MeNH)<sub>2</sub>CO with NCCH<sub>2</sub>CO<sub>2</sub>H in Ac<sub>2</sub>O 12 hr at 80.degree. to yield 72% I, m. 275.degree. (decompn.). I and 3-C<sub>5</sub>H<sub>4</sub>NCH<sub>2</sub>CO<sub>2</sub>H refluxed 3 hr in PhNMe<sub>2</sub> under a Dean-Stark head yielded II, m. 291-5.degree.. Coupling with Me<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>Cl, HOCH<sub>2</sub>CH<sub>2</sub>Cl, HOCH<sub>2</sub>CH(OH)CH<sub>2</sub>Cl, HO<sub>2</sub>CCH<sub>2</sub>Cl, and H<sub>2</sub>C:CHCN gave the corresponding 7-substituted II. Catalytic hydrogenation of 7-(2-cyanoethyl)-8-(3-pyridylmethyl)theophylline in MeOH with Raney Co in liq. NH<sub>3</sub> gave 7-(3-aminopropyl)-8-(3-pyridylmethyl)-theophylline.
- IT 28345-99-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prep. of)
- RN 28345-99-5 HCAPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinylmethyl)- (9CI)  
 (CA INDEX NAME)

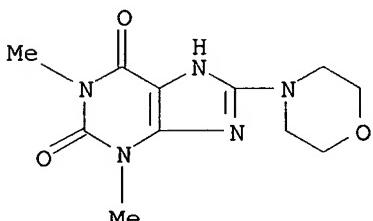


- L5 ANSWER 149 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
 1971:87924 Document No. 74:87924 Synthesis of 1- and 7-.beta.-hydroxypropyl-8-cycloalkylaminodimethylxanthines. Gorczyca, Maria; Mogilnicka, Ewa; Wantuch, Czeslawa (Dep. Pharm. Chem., Med. Acad., Cracow, Pol.). Diss. Pharm. Pharmacol., 22(6), 403-10 (English) 1970. CODEN: DPHFAK.
- GI For diagram(s), see printed CA Issue.
- AB Xanthines (I and II; R = H, R<sub>1</sub> = morpholino, piperidino, pyrrolidino) were prepd. in 85-90 yield by treating 8-bromotheobromine and 8-bromotheophylline, resp., with a 4-fold excess of the amine. Treatment of I and II (R = H) with 2,3-epoxypropane and pyridine gave 70-80% I and II (R = CH<sub>2</sub>CHMeOH). II (R = CH<sub>2</sub>CHMeOH, R<sub>1</sub> = morpholino or piperidino) were also prepd. by allylating the corresponding II (R = H) and hydrating the products.
- IT 961-48-8P 30958-49-7P 30958-51-1P

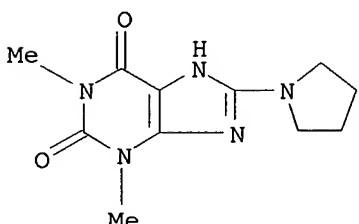
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of)  
RN 961-48-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinyl)- (9CI)  
(CA INDEX NAME)



RN 30958-49-7 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-morpholinyl)- (9CI)  
(CA INDEX NAME)



RN 30958-51-1 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-pyrrolidinyl)- (9CI)  
(CA INDEX NAME)



L5 ANSWER 150 OF 163 HCAPLUS COPYRIGHT 2002 ACS  
1971:21695 Document No. 74:21695 Pharmacodynamic study of derivatives of  
.gamma.- (3-pyridylmethyl)theophylline. Debaert, Michel; Laude, F.;  
Minard-Vaillant, Mrs.; Robelet, Alfred (Lab. Physiol. Appl. Pharmacol.,  
Fac. Med., Lille, Fr.). Therapie, 25(4), 683-706 (French) 1970. CODEN:  
THERAP.  
GI For diagram(s), see printed CA Issue.  
AB The antispasmodic and hypotensive activities of 6 theophylline derivs.  
with a methylpyridyl group at C-8, such as 7-(2-hydroxyethyl)-8-(3-  
pyridylmethyl)theophylline (mouse LD50 = 140 mg/kg, i.v.) and  
7-(2,3-dihydroxypropyl)-8-(3-phryidylmethyl)-theophylline (mouse LD50 =  
190 mg/kg, i.v.), were studied. With the exception of

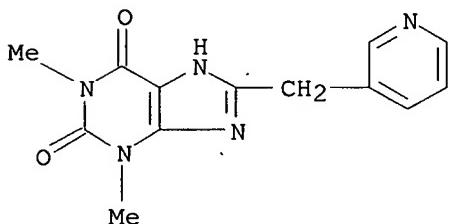
7-(carboxymethyl)-8-(3-pyridylmethyl)-theophylline (I) (mouse LD<sub>50</sub> = 500 mg/kg, i.v.), the derivs. had a greater neurotropic antispasmodic activity in the isolated guinea pig intestine than aminophylline, and a comparable musculotropic antispasmodic activity and antagonistic effect against histamine-induced spasms. In the guinea pig gall bladder there was no significant difference between the antispasmodic activity of aminophylline and the derivs., with the exception of I. The antispasmodic activity of 8-(3-pyridylmethyl)theophylline (II) (mouse LD<sub>50</sub> = 250 mg/kg, i.v.) and 7-(3-aminopropyl)-8-(3-pyridylmethyl)theophylline (mouse LD<sub>50</sub> = 48 mg/kg, i.v.) was greater than or at least equal to that of aminophylline in the biliary system of guinea pigs treated with carbamylcholine. In vivo the activity of the derivs. against histamine-induced bronchospasm was less than that of aminophylline. The theophylline derivs. had a hypotensive activity in rats which was less than that of aminophylline. Although the 3-pyridylmethyl group at C-8 is favorable for antispasmodic and hypotensive activity, substituents at C-7 which increase solv. lessen the pharmacodynamic activity.

IT 28345-99-5

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmacology of)

RN 28345-99-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinylmethyl)- (9CI)  
(CA INDEX NAME)



L5 ANSWER 151 OF 163 HCPLUS COPYRIGHT 2002 ACS

1971:19728 Document No. 74:19728 Determination of the inhibitory activity of some substituted theophyllines on the phosphodiesterase specific for the adenosine 3',5'-monophosphate. Lespagnol, Albert; Debaert, Michel; Mizon, Jacques; Mizon-Capron, Charlotte (Lab. Pharm. Chim. Chim. Biol., U.E.R. Pharm., Lille, Fr.). Therapie, 25(4), 707-13 (French) 1970. CODEN: THERAP.

GI For diagram(s), see printed CA Issue.

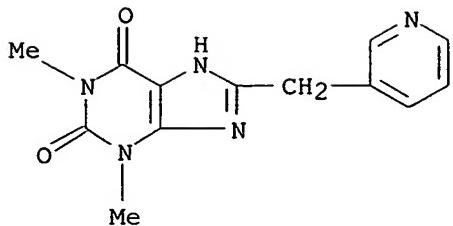
AB The inhibitory effect of 6 theophylline derivs., including I, II, and III, on phosphodiesterase activity during cy-clic-AMP hydrolysis was studied in vitro. The effects of all the derivs. were between those of caffeine and theophylline. The presence of a side chain at N-7 decreased the inhibitory activity. Comparison between antispasmodic activity, evaluated in guinea pig bronchus in a previous study, and phosphodiesterase activity indicated that phosphodiesterase activity may be useful for preselection of compds. with theophyllinic-type activity prior to pharmacol. testing.

IT 28345-99-5

RL: BIOL (Biological study)  
(adenosine cyclic phosphate phosphodiesterase inhibition by)

RN 28345-99-5 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinylmethyl)- (9CI)  
(CA INDEX NAME)



L5 ANSWER 152 OF 163 HCAPLUS COPYRIGHT 2002 ACS

1970:520677 Document No. 73:120677 Substituted purines and purine derivatives and their biologically and pharmacologically active compositions. Bergmann, Felix G.; Kleiner, Mordechai A.; Rashi, Moshe (Yissum Research Development Co. of the Hebrew University of Jerusalem). Brit. GB 1201997 19700812, 21 pp. (English). CODEN: BRXXAA. PRIORITY: IL 19670804.

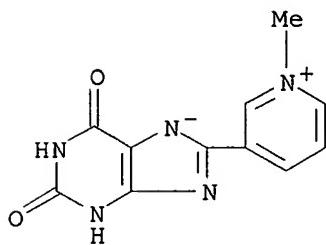
AB Antitumor-active 8-(2-, 3-, and 4-pyridyl) purines are prep'd. from 4,5-diaminopyrimidines and amidinium salts. Thus, a mixt. of 4,6-diamino-6-hydroxypyrimidine, 3-amidinopyridine-HCl, and anhyd. NaOAc was heated 15 min at 190.degree. to give 81% 8-(3-pyridyl)hypoxanthine, m. >310.degree.. Similarly prep'd. were 8-(3-pyridyl)xanthine (I) and 10 other I analogs. I was converted into the methiodide by heating with MeI in DMF 6 hr at 50.degree.. Treatment of a warm aq. soln. of the salt with NH4OH gave 8-(3-N-methylpyridinium)xanthine betaine-0.5 H2O, m. 310.degree. (decompn.). Similarly prep'd. were 3-methyl-6-methylthio-8-[4-(N-methyl)pyridinio]purine iodide (II) and 6 other II analogs. II was treated with a soln. of NH4OH satd. with H2S 0.5 hr at 0.degree. to give 30% 3-methyl-8-(4-N-methylpyridinio)-6-mercaptopurine betaine (III). I.v. injection of 8-pyridylxanthines, 3-methyl-6-methylthio-8-(2-pyridyl)purine, II, and III into a nembutalized cat produced marked and prolonged hypotension. The 8-pyridyl-6-mercaptopurines and their S-methyl ethers when dosed i.p. produced inhibition of EO 771 mammary adenocarcinoma, S-180 sarcoma and Ehrlich ascites carcinoma in mice.

IT 12212-19-0P 12212-20-3P 15846-80-7P  
15846-81-8P 15846-82-9P 15846-94-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

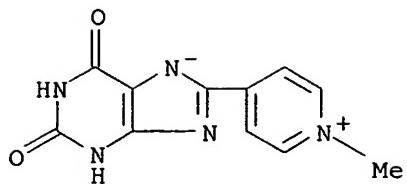
RN 12212-19-0 HCAPLUS

CN Pyridinium, 1-methyl-3-(1,2,3,6-tetrahydro-2,6-dioxopurin-8-yl)-, hydroxide, inner salt (8CI) (CA INDEX NAME)

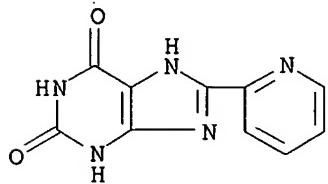


RN 12212-20-3 HCAPLUS

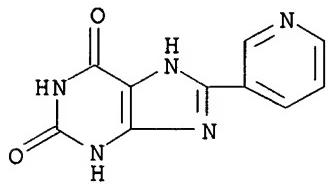
CN Pyridinium, 1-methyl-4-(1,2,3,6-tetrahydro-2,6-dioxopurin-8-yl)-, hydroxide, inner salt (8CI) (CA INDEX NAME)



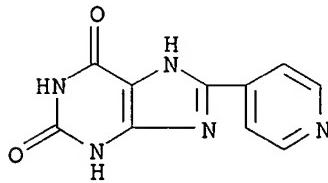
RN 15846-80-7 HCAPLUS  
CN Xanthine, 8-(2-pyridyl)- (8CI) (CA INDEX NAME)



RN 15846-81-8 HCAPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



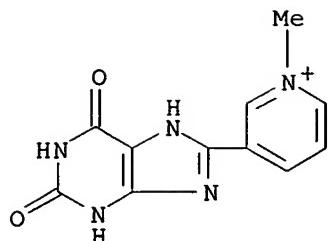
RN 15846-82-9 HCAPLUS  
CN Xanthine, 8-(4-pyridyl)- (8CI) (CA INDEX NAME)



RN 15846-94-3 HCAPLUS  
CN Pyridinium, 1-methyl-3-(1,2,3,6-tetrahydro-2,6-dioxopurin-8-yl)-, picrate (8CI) (CA INDEX NAME)

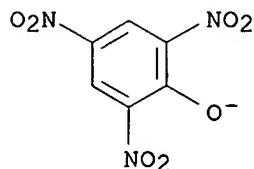
CM 1

CRN 46891-31-0  
CMF C11 H10 N5 O2



CM 2

CRN 14798-26-6  
CMF C6 H2 N3 O7



L5 ANSWER 153 OF 163 HCPLUS COPYRIGHT 2002 ACS

1970:498907 Document No. 73:98907 New purine synthesis. Yoneda, Fumio; Ogiwara, Kazuko; Kanahori, Michiko; Nishigaki, Sadao (Sch. Med., Keio Univ., Tokyo, Japan). J. Chem. Soc. D (17), 1068-9 (English) 1970.  
CODEN: CCJDAO.

GI For diagram(s), see printed CA Issue.

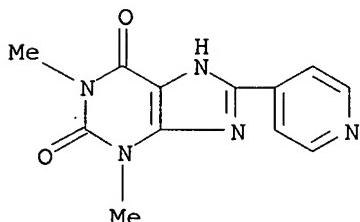
AB The 5-nitrosouracil compd., I (R = Me, R1 = H), is treated with hydrazones ArCH:N(R2)2 (R2 = H, Me) to give theophyllines II (R = Me, Ar = aryl). 1,9-Dimethylxanthines II (R = H, R1 = Me) are prep'd. from I (R = H, R1 = Me).

IT 1088-64-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep'n. of)

RN 1088-64-8 HCPLUS

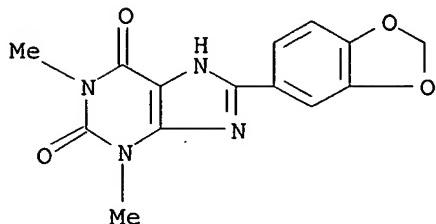
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



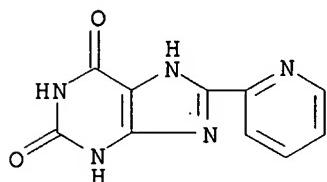
L5 ANSWER 154 OF 163 HCPLUS COPYRIGHT 2002 ACS

1969:4017 Document No. 70:4017 8-Aryltheophyllines. Bariana, D. S. (Res. Dep., Abbott Lab. Ltd., Montreal, Que., Can.). Can. J. Chem., 46(21),

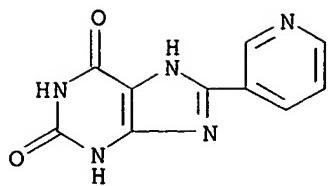
3413-15 (English) 1968. CODEN: CJCHAG.  
 AB The synthesis of a no. of 8-aryltheophyllines is described. These compds. were tested as coronary vasodilators.  
 IT 20886-69-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepns. of)  
 RN 20886-69-5 HCPLUS  
 CN 1H-Purine-2,6-dione, 8-(1,3-benzodioxol-5-yl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



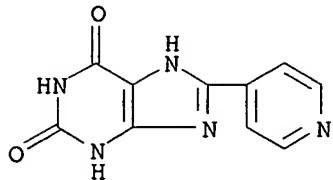
L5 ANSWER 155 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1967:464361 Document No. 67:64361 Synthesis and properties of 8-pyridylpurines. Bergmann, Felix; Rashi, Moshe; Kleiner, Mordechai; Knafo, R. (Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel). J. Chem. Soc. C (13), 1254-60 (English) 1967. CODEN: JSOOAX.  
 GI For diagram(s), see printed CA Issue.  
 AB 8-Pyridylpurines, such as I, were synthesized by condensation of 4,5-diaminopyrimidines with amidinopyridines. Protonation of the pyridine N causes a marked bathochromic shift of  $\lambda_{\text{max}}$ . in the 2- and 4-pyridyl derivs., but not in the 3-pyridyl isomers. A similar effect is produced by quaternization of the 4-, but not of the 3-pyridyl substituent, while quaternization of 8-(2-pyridyl)purines has not been achieved so far. The 8-(1-methyl)pyridinium group also greatly facilitates anion formation in the purine ring. 18 references.  
 IT 15846-80-7P 15846-81-8P 15846-82-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepns. of)  
 RN 15846-80-7 HCPLUS  
 CN Xanthine, 8-(2-pyridyl)- (8CI) (CA INDEX NAME)



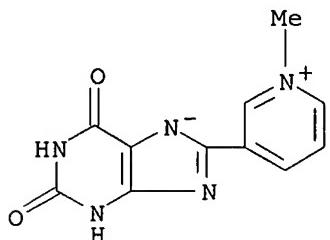
RN 15846-81-8 HCPLUS  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



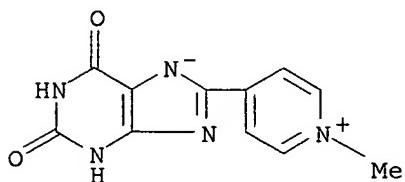
RN 15846-82-9 HCAPLUS  
CN Xanthine, 8-(4-pyridyl)- (8CI) (CA INDEX NAME)



IT 12212-19-0P 12212-20-3P 15846-94-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prep., acidity and spectrum (uv) of)  
RN 12212-19-0 HCAPLUS  
CN Pyridinium, 1-methyl-3-(1,2,3,6-tetrahydro-2,6-dioxopurin-8-yl)-,  
hydroxide, inner salt (8CI) (CA INDEX NAME)



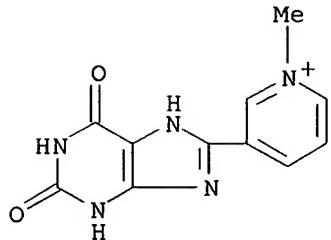
RN 12212-20-3 HCAPLUS  
CN Pyridinium, 1-methyl-4-(1,2,3,6-tetrahydro-2,6-dioxopurin-8-yl)-,  
hydroxide, inner salt (8CI) (CA INDEX NAME)



RN 15846-94-3 HCAPLUS  
CN Pyridinium, 1-methyl-3-(1,2,3,6-tetrahydro-2,6-dioxopurin-8-yl)-, picrate  
(8CI) (CA INDEX NAME)

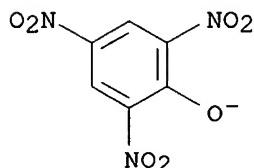
CM 1

CRN 46891-31-0  
CMF C11 H10 N5 O2



CM 2

CRN 14798-26-6  
CMF C6 H2 N3 O7



L5 ANSWER 156 OF 163 HCPLUS COPYRIGHT 2002 ACS

1965:424146 Document No. 63:24146 Original Reference No. 63:4296b-h,4297a-b  
Purine derivatives. IV. Synthesis of bistheophyllines containing sulfur  
and of methylated thiouric acid derivatives. Merz, K. W.; Stahl, P. H.  
(Univ. Freiburg/Br., Germany). Arzneimittel-Forsch., 15(1), 10-14  
(German) 1965.

GI For diagram(s), see printed CA Issue.

AB cf. CA 55, 1626f; 61, 8309b. HCONMe<sub>2</sub> (80 ml.) contg. 3.4 g.  
6-thiotheophylline K salt (I) treated dropwise in 50 min. at 135.degree.  
(oil bath) with 1.25 g. CH<sub>2</sub>Br<sub>2</sub> in 50 ml. HCONMe<sub>2</sub> with stirring, the mixt.  
stirred 1 hr. at 135.degree., and the product washed with H<sub>2</sub>O yielded  
71.4% bis(thiotheophylline) (II) (R = CH<sub>2</sub>), m. 345-6.degree. (decompn.).  
Similarly were prep'd. the corresponding II [R = (CH<sub>2</sub>)<sub>2</sub>, (CH<sub>2</sub>)<sub>3</sub>,  
trans-CH<sub>2</sub>CH:CHCH<sub>2</sub>, and dl-erythro-CH<sub>2</sub>(CHOH)2CH<sub>2</sub>], m. 335, 311-17,308,  
325-7.degree. (all with decompn.), resp. Treatment of 3.5 g. I with 1.4  
g. Br(CH<sub>2</sub>)<sub>2</sub>Br in moist HCONMe<sub>2</sub> and the filtered soln. evapd. in vacuo to  
50 ml. yielded 1.8% 7-(.beta.-hydroxyethyl)-6-thiotheophylline, m.  
236-40.degree. (decompn.). H<sub>2</sub>C(CONH<sub>2</sub>)<sub>2</sub> (1.2 g.) and 4.0 g.  
1,3-dimethyl-4,5-diaminouracil (III) refluxed 6.5 hrs. at 196.degree. in  
60 ml. HOCH<sub>2</sub>CH<sub>2</sub>OH and the mixt. refluxed 3.5 hrs. with 0.4 g. addnl.  
H<sub>2</sub>C(CONH<sub>2</sub>)<sub>2</sub>, filtered, and the residue washed with hot H<sub>2</sub>O, alc., and  
CHCl<sub>3</sub> gave di-(8-theophyllinyl)methane (IV) (R = CH<sub>2</sub>, Y = Z = O), giving a  
bright blue fluorescence at .lambda., 366 m.mu.. Similarly were produced  
from III and the 2-thio analog. by treatment with H<sub>2</sub>C(CONH<sub>2</sub>)<sub>2</sub> and  
(H<sub>2</sub>CCONH<sub>2</sub>)<sub>2</sub> the corresponding C-8, C-8'-bistheophylline compds. IV [R =  
(CH<sub>2</sub>)<sub>2</sub>, Y = Z = O; R = CH<sub>2</sub>, Y = O, Z = S; R = (CH<sub>2</sub>)<sub>2</sub>, Y = O, Z = S], m.  
above 400.degree., giving bright blue, greenish blue, and greenish

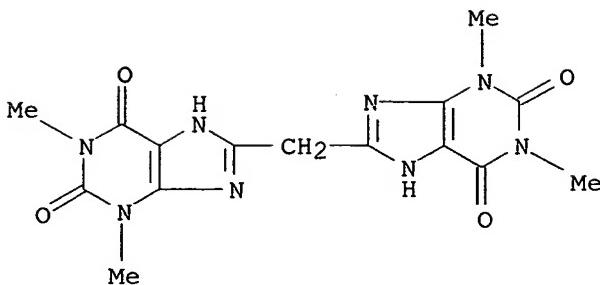
fluorescence, resp. IV were insol. in the usual org. solvents and attempts to purify the compds. by recovery from acid soln. failed. No picrate or perchlorate salts were formed and IV were characterized by comparison of uv spectra with those of theophylline and 2-thiotheophylline in buffer soln. at pH 11.0 and in MeOH. The thio analogs [(V) (Y = O, Z = S; Y = S, Z = O; Y = Z = S) (VI, VII, VIII)] of III served as starting material for the previously unknown .delta.-thiouric acid derivs. IX (X = O, Y = S; X = S, Y = O; X = Y = S) (X, XI, XII). VI (2.0 g.) and 10 g. (H<sub>2</sub>N)<sub>2</sub>CS intimately mixed and heated 10-15 min. at 185-90.degree. (metal bath), and the cooled melt taken up in dil. NH<sub>4</sub>OH, treated with C, and the filtered alk. soln. acidified with 2N HCl to pH 3-4 yielded X, m. 315-22.degree. (decompn.) (HCONMe<sub>2</sub>-H<sub>2</sub>O), taken up in 2% aq. borax soln. and treated with 2,6-dichloroquinone-4-chlorimide to give an immediate intense violet color, .lambda. 240, 320 m.mu. (.epsilon. 18,800, 25,000, NaOH-glycine buffer, pH 11.0), .lambda. 240, 311.5 m.mu. (.epsilon. 15,500, 22,200, MeOH). KOH (2.0 g.), 3.5 g. CS<sub>2</sub>, and 5.0 g. VI in 5 ml. H<sub>2</sub>O and 80 ml. alc. refluxed 5.5 hrs. the mixt. dild. with H<sub>2</sub>O, and the clear soln. acidified with 2N HCl also gave X. VI (2.5 g.) heated with 12 g. (MeNH)<sub>2</sub>CS and the melt processes as above similarly gave X in 75% yields. Heating VII and VIII with (H<sub>2</sub>N)<sub>2</sub>CS as for VI gave the corresponding XI, m. 327-9.degree. (decompn.), and XII, m. 304-10.degree. (gas evolution). VI (1.0 g.) and 8.0 g. (MeNH)<sub>2</sub>CS melted 5 min. at 260-70.degree. and the cooled melt stirred with H<sub>2</sub>O, acidified with 2N HCl, and the H<sub>2</sub>O-washed product recrystd. from HCONMe<sub>2</sub> yielded 89.7% 8-methylthio-2-thiotheophylline, m. 338-40.degree., .lambda. 236, 306 m.mu. (.epsilon. 21,600, 23,200, pH 11.0), .lambda. 238, 301 m.mu. (.epsilon. 17,500, 21,600, MeOH), also produced by methylation of X. Similarly, 2.5 g. III and 8 g. (H<sub>2</sub>N)<sub>2</sub>CS, 2.5 g. III, and 8 g. (MeNH)<sub>2</sub>CS, or 2.5 g. 1,3-dimethyl-4-methylamino-5-aminouracil (XIII) and 8 g. (H<sub>2</sub>N)<sub>2</sub>CS gave 71, 70, or 62% crude product, recrystd. to give 8-mercaptoptheophylline (XIV), m. 322-4.degree., giving an immediate intense violet color with 2,6-dichloroquinone-4-chlorimide, .lambda. 235, 312 m.mu. (.epsilon. 17,400, 23,100, pH 11.0), .lambda. 226, 805.5 m.mu. (.epsilon. 11,100, 18,400, MeOH). III (1.0 g.) heated with 5.0 g. (MeNH)<sub>2</sub>CS 5 min. at 260-70.degree. and the product isolated yielded 8-methylthiotheophylline, m. 314.degree., giving no color reaction, .lambda. 225, 295 m.mu. (.epsilon. 15,700, 16,850, pH 11.0), .lambda. 291.5 m.mu. (.epsilon. 17,300, MeOH), also obtained by methylation of XIV. XIII (1.8 g.) and 0.7 g. KOH refluxed with 5 ml. H<sub>2</sub>O and 3 ml. CS<sub>2</sub> 1 hr. in 50 ml. alc., and the product taken up in H<sub>2</sub>O and acidified with 2N HCl gave 1,3,9-trimethyl-8-thiouric acid, m. 331-5.degree. (decompn.), giving yellow flocculation with 2,6-dichloroquinone-4-chlorimide, .lambda. 265, 306 m.mu. (.epsilon. 14,200, 11,200, pH 11.0), .lambda. 271,309 m.mu. (.epsilon. 11,200, 11,700, MeOH).

IT 1784-51-6, Theophylline, 8,8'-methylenedi- 1784-67-4,  
Theophylline, 8,8'-ethylenedi-

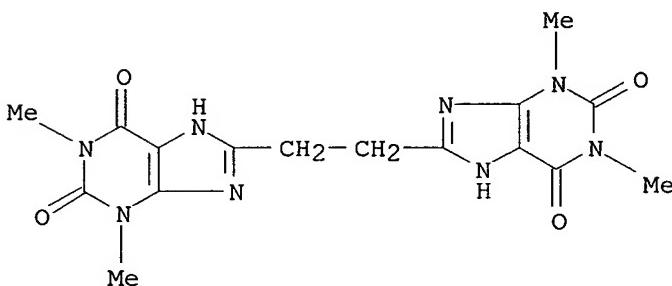
(prepn. of)

RN 1784-51-6 HCPLUS

CN 1H-Purine-2,6-dione, 8,8'-methylenebis[3,7-dihydro-1,3-dimethyl- (9CI)  
(CA INDEX NAME)

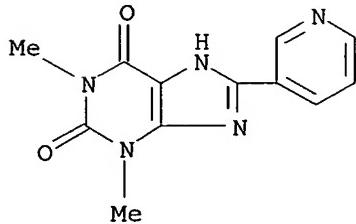


RN 1784-67-4 HCPLUS  
 CN 1H-Purine-2,6-dione, 8,8'-(1,2-ethanediyl)bis[3,7-dihydro-1,3-dimethyl-  
 (9CI) (CA INDEX NAME)

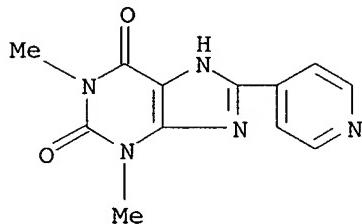


L5 ANSWER 157 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1965:18106 Document No. 62:18106 Original Reference No. 62:3280g-h,3281a-b  
 8-Pyridyltheophyllines; chemical and pharmacological data. Casagrande,  
 C.; Ferrari, G.; Bergamaschi, M.; Marchetti, G. (Simes S.p.A., Milan).  
*Boll. Chim. Farm.*, 103(9), 641-52 (Italian) 1964.  
 AB Isonicotinoyl chloride hydrochloride (prepd. from 41 g. isonicotinic acid)  
 was added portionwise, with stirring, to a suspension of 57 g.  
 1,3-dimethyl-5,6-diaminouracil in 420 ml. dry pyridine maintained at  
 20.degree.. The mixt. was stirred overnight at room temp., heated at  
 100.degree. for 5 hrs., dild. with little H2O, neutralized with NaHCO3,  
 evapd. to dryness in vacuo, the residue mixed with little H2O, evapd.  
 again, dissolved in hot H2O, adjusted to pH 8 with Na2CO3, let stand in a  
 refrigerator, filtered, and crystd. from H2O to yield 54 g. (60%)  
 5-isonicotamido-6-amino-1,3-dimethyluracil (I). By the analogous  
 procedure nicotinoyl chloride hydrochloride (prepd. from 43 g. nicotinic  
 acid) yielded 52.5 g. (58%) 5-nicotinamido-6-amino-1,3-dimethyluracil  
 (II). I (27.5 g.) heated 10 min. at 285.degree., the cooled product  
 dissolved in 2% NaOH, treated with charcoal, filtered, and the filtrate  
 satd. with CO2 to yield 22 g. (85%) 8.gamma.-pyridyltheophylline (III)  
 crystd. from dimethylformamide. III triturated with dil. HCl yielded  
 III.HCl, yellow crystals; insol. cold H2O, m. >320.degree. (dil. HCl).  
 8.beta.-pyridyltheophylline (IV) was similarly prepd. from II, with the  
 difference of keeping the soln. warm during CO2 satn. By triturating with  
 dil. HCl IV gave IV.HCl, white crystals, insol. in cold H2O, m.  
 >320.degree. (50% AcOH + little HCl). Both products showed marked  
 analeptic and bronchodilator actions, similar to those induced by equal  
 doses of aminophylline (V). When orally administrated or subcutaneously  
 injected, III and IV were less toxic, when intravenously injected as toxic  
 as V. L.D.50 in mice was, resp., 790 and 1000 orally, and 110 and 158

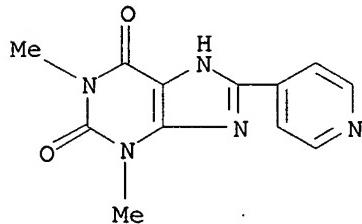
mg./kg. intravenously.  
IT 1029-62-5, Theophylline, 8-(3-pyridyl)- 1088-64-8,  
Theophylline, 8-(4-pyridyl)-  
(prep. and pharmacology of)  
RN 1029-62-5 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 1088-64-8 HCPLUS  
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)

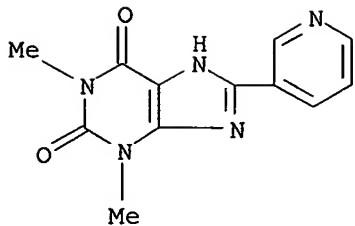


IT 3321-41-3, Theophylline, 8-(4-pyridyl)-, hydrochloride  
95593-45-6, Theophylline, 8-(3-pyridyl)-, hydrochloride  
(prep. of)  
RN 3321-41-3 HCPLUS  
CN Theophylline, 8-(4-pyridyl)-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 95593-45-6 HCPLUS  
CN Theophylline, 8-(3-pyridyl)-, hydrochloride (7CI) (CA INDEX NAME)



● HCl

L5 ANSWER 158 OF 163 HCPLUS COPYRIGHT 2002 ACS

1965:9121 Document No. 62:9121 Original Reference No. 62:1661f-h Synthesis of 8-substituted theophyllines. Isolation of a 7-N-oxide intermediate and an unusual Leukart reduction with dimethylformamide. Taylor, Edward C.; Garcia, Edward E. (Princeton Univ., Princeton, NJ). J. Am. Chem. Soc., 86(21), 4721-2 (English) 1964. CODEN: JACSAT. ISSN: 0002-7863.

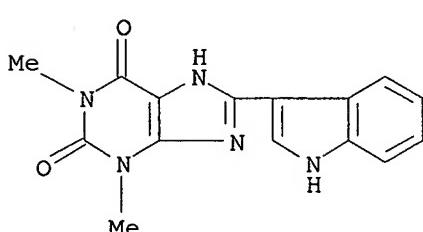
GI For diagram(s), see printed CA Issue.

AB cf. preceding abstr. 1,3-Dimethyl-4-amino-5-nitrosouracil (I) and BzH in HCONMe<sub>2</sub> gave 8-phenyltheophylline (II). Concn. of the filtrate gave III, decompn. above 169.degree., which methylated with Me<sub>2</sub>SO<sub>4</sub> and NaOH gave IV. Catalytic redn. of IV gave II. Heating III in HCONMe<sub>2</sub> gave II and Me<sub>2</sub>NH. Addn. of HCO<sub>2</sub>H (as reducing agent) in the reaction of I and BzH gave 1,3,6,8-tetramethyl-2,4,5,7(1H,3H,6H,8H)-pyrimido[5,4-g]pteridinetetrone (V), less II, and no III. I and indole-3-carboxaldehyde, 1-C<sub>10</sub>H<sub>7</sub>CHO, p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CHO, and .omicron.-MeOC<sub>6</sub>H<sub>4</sub>CHO in HCONMe<sub>2</sub> and HCO<sub>2</sub>H gave the corresponding 8-substituted theophyllines, m. >360, 328-9, >360, >360.degree., resp. I and BzCHO and HCO<sub>2</sub>H, however, gave 1,3-dimethyl-4-amino-5-benzamidouracil, m. 287-9.degree., and 1,3-dimethyl-7-phenyl-2,4(1H,3H)pteridinedione. The reaction mechanism is discussed.

IT 970-84-3, Theophylline, 8-indol-3-yl- 973-39-7,  
Theophylline, 8-(3-methylindol-1-yl)-  
(prepn. of)

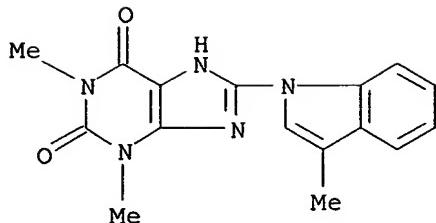
RN 970-84-3 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-8-(1H-indol-3-yl)-1,3-dimethyl- (9CI)  
(CA INDEX NAME)



RN 973-39-7 HCPLUS

CN Theophylline, 8-(3-methylindol-1-yl)- (7CI, 8CI) (CA INDEX NAME)



L5 ANSWER 159 OF 163 HCPLUS COPYRIGHT 2002 ACS

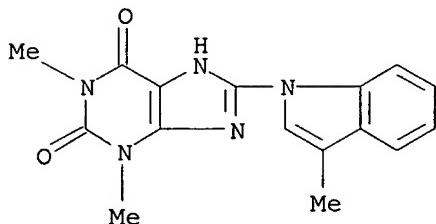
1965:9120 Document No. 62:9120 Original Reference No. 62:1661e-f A new purine synthesis. Taylor, Edward C.; Garcia, Edward E. (Princeton Univ., Princeton, NJ). J. Am. Chem. Soc., 86(21), 4720-1 (English) 1964. CODEN: JACSAT. ISSN: 0002-7863.

AB Condensation of 1,3-dimethyl-4-amino-5-nitrosouracil (I) with Me<sub>3</sub>(PhCH<sub>2</sub>)NI in refluxing HCONMe<sub>2</sub> gave 31% 8-phenyltheophylline and Me<sub>3</sub>N. When the appropriate quaternized Mannich bases were used 8-(3-methyl-1-indolyl)- and 8-(3-methyl-2-hydroxyphenyl)-theophylline were obtained. Similar condensation of I with gramine gave 8-(3-indolyl)theophylline. The reaction mechanism is discussed.

IT 973-39-7, Theophylline, 8-(3-methylindol-1-yl)-  
(prep. of)

RN 973-39-7 HCPLUS

CN Theophylline, 8-(3-methylindol-1-yl)- (7CI, 8CI) (CA INDEX NAME)



L5 ANSWER 160 OF 163 HCPLUS COPYRIGHT 2002 ACS

1965:9118 Document No. 62:9118 Original Reference No. 62:1660f-h Chemical and pharmacodynamic study of 8-piperidyltheophyllines. Pesson, Marcel; Bathellier, Colette; Kornowski, Henri; Auroousseau, Michel (School Med., Rheims). Ann. Pharm. Franc., 22;22(3;4), 17-93;265-73 (French) 1964.

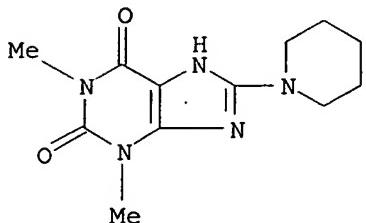
AB Condensation of 1,3-dimethyl-4,5-diaminouracil (I) with the corresponding pyridinecarboxylic acids yield the following 8-theophylline derivs.: 2-pyridyl (II), 3-pyridyl (III) and 4-pyridyl (IV). Catalytic hydrogenation of II, III, and IV yields the corresponding piperidyl derivs. Catalytic hydrogenation of IV in the presence of aldehydes yields (N-methyl-4-piperidyl) (VI) and (N-ethyl-4-piperidyl)-8-theophylline (VII). Condensation of 8-bromotheophylline and piperidine yields 8-(N-piperidyl)theophylline (VIII). The toxicity, cardiovascular, spasmolytic, and diuretic activity of the H<sub>2</sub>O-sol. derivs. (II, III, IV, VI, and VIII) were detd. All showed lesser activity than theophylline.

IT 961-48-8, Theophylline, 8-piperidino- 964-56-7,  
Theophylline, 8-(1-methyl-4-piperidyl)-, hydrochloride 967-40-8,  
Theophylline, 8-(1-nitroso-2-piperidyl)- 967-41-9, Theophylline,  
8-(1-nitroso-3-piperidyl)- 1029-62-5, Theophylline,  
8-(3-pyridyl)- 1088-64-8, Theophylline, 8-(4-pyridyl)-

**1088-65-9**, Theophylline, 8-(2-pyridyl)- 1090-62-6,  
Theophylline, 8-(1-methyl-4-piperidyl)- 1092-48-4, Theophylline,  
8-(1-ethyl-4-piperidyl)- 2052-35-9, Theophylline,  
8-(1-nitroso-4-piperidyl)- 96434-25-2, Theophylline,  
8-(2-piperidyl)-, hydrochloride 96434-26-3, Theophylline,  
8-(3-piperidyl)-, hydrochloride 96434-27-4, Theophylline,  
8-(4-piperidyl)-, hydrochloride 97361-19-8, Theophylline,  
8-(1-ethyl-4-piperidyl)-, hydrochloride  
(prepn. of)

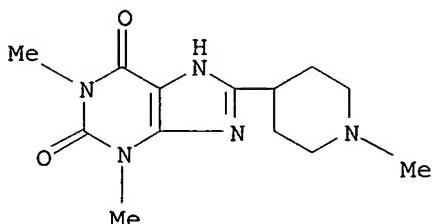
RN 961-48-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(1-piperidinyl)- (9CI)  
(CA INDEX NAME)



RN 964-56-7 HCAPLUS

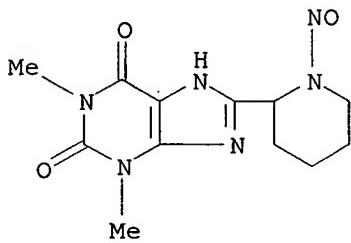
CN Theophylline, 8-(1-methyl-4-piperidyl)-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

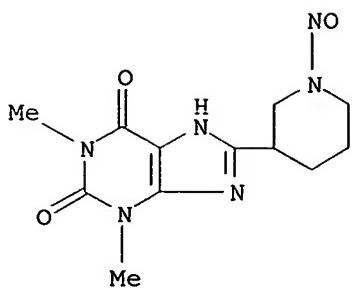
RN 967-40-8 HCAPLUS

CN Theophylline, 8-(1-nitroso-2-piperidyl)- (8CI) (CA INDEX NAME)



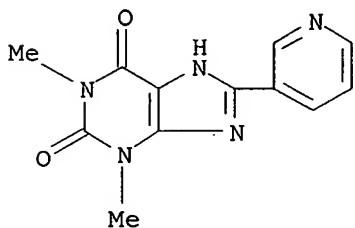
RN 967-41-9 HCAPLUS

CN Theophylline, 8-(1-nitroso-3-piperidyl)- (8CI) (CA INDEX NAME)



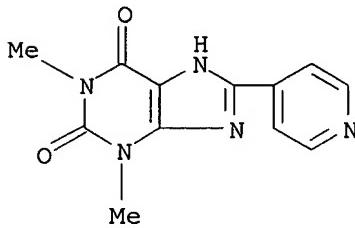
RN 1029-62-5 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(3-pyridinyl)- (9CI) (CA INDEX NAME)



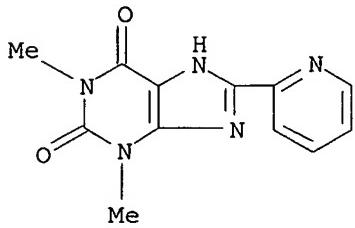
RN 1088-64-8 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(4-pyridinyl)- (9CI) (CA INDEX NAME)



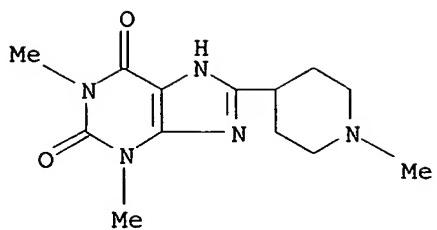
RN 1088-65-9 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-(2-pyridinyl)- (9CI) (CA INDEX NAME)



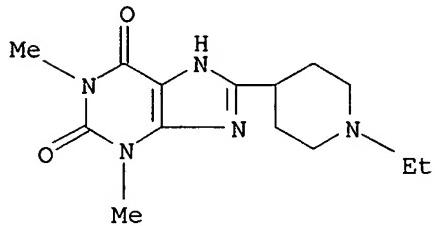
RN 1090-62-6 HCAPLUS

CN Theophylline, 8-(1-methyl-4-piperidyl)- (7CI, 8CI) (CA INDEX NAME)



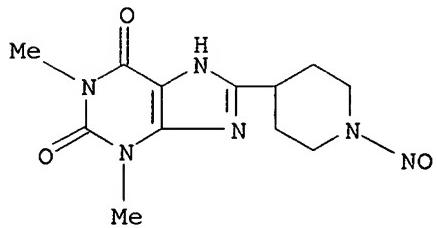
RN 1092-48-4 HCPLUS

CN Theophylline, 8-(1-ethyl-4-piperidyl)- (7CI, 8CI) (CA INDEX NAME)



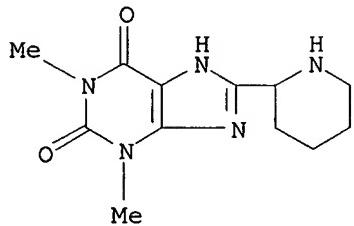
RN 2052-35-9 HCPLUS

CN Theophylline, 8-(1-nitroso-4-piperidyl)- (8CI) (CA INDEX NAME)



RN 96434-25-2 HCPLUS

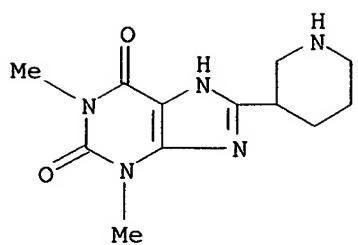
CN Theophylline, 8-(2-piperidyl)-, hydrochloride (7CI) (CA INDEX NAME)



●x HCl

RN 96434-26-3 HCPLUS

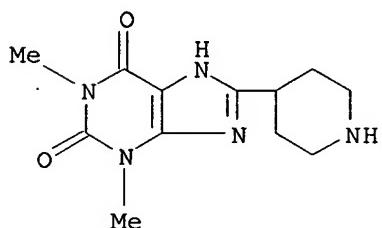
CN Theophylline, 8-(3-piperidyl)-, hydrochloride (7CI) (CA INDEX NAME)



●x HCl

RN 96434-27-4 HCPLUS

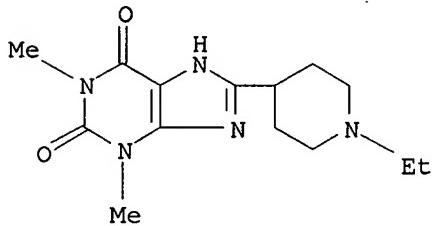
CN Theophylline, 8-(4-piperidyl)-, hydrochloride (7CI) (CA INDEX NAME)



●x HCl

RN 97361-19-8 HCPLUS

CN Theophylline, 8-(1-ethyl-4-piperidyl)-, hydrochloride (7CI) (CA INDEX NAME)



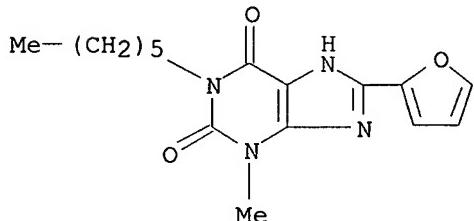
●x HCl

L5 ANSWER 161 OF 163 HCPLUS COPYRIGHT 2002 ACS

1962:73525 Document No. 56:73525 Original Reference No. 56:14305e-h

8-Substituted-1,3-dialkylxanthines. Schuh, Heinz Georg v. (Chemische Werke Albert). DE 1091570 19601027 (Unavailable). APPLICATION: DE 19581023.

- GI For diagram(s), see printed CA Issue.
- AB The title compds. were prep'd. for drug use. Adding 2 g. NaOH to 20 g. PhCH<sub>2</sub>CO<sub>2</sub>H at 150.degree., the formed H<sub>2</sub>O evapd. in vacuo, 10 g. 8-bromotheophylline added, the whole heated 1.5 hrs. at 210-15.degree. (CO<sub>2</sub> evolved), poured in 200 cc. H<sub>2</sub>O and 80 cc. 4N NaOH, treated with C, filtered, and CO<sub>2</sub> bubbled through the filtrate gave 81% brown 8-benzyltheophylline, m. 292.degree. (AcOH or Na<sub>2</sub>CO<sub>3</sub> soln.). The following derivs. of 3-methylxanthine were prep'd. from suitable 8-halo theophyllines (deriv., yield, m.p., crystn. solvent, and other reactants given): 1,8-Bu(m-MeOC<sub>6</sub>H<sub>4</sub>), 80%, 246-9.degree., Na<sub>2</sub>CO<sub>3</sub> soln., m-MeOC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>H, KOH; 8,1-iso-Pr(Me<sub>2</sub>CHCH<sub>2</sub>CH<sub>2</sub>), 97%, 150-2.degree., MeOH, Me<sub>2</sub>CHCO<sub>2</sub>K, (Me<sub>2</sub>CHCO)<sub>2</sub>O; 1,8-hexyl(.alpha.-furyl), 78%, 220-2.degree., alc., I, II; 1,8-hexyl(.delta.-carboxybutyl), 93%, 167-71.degree., iso-PrOH, Na adipate, adipic acid; 1,8-hexyl(PhCH<sub>2</sub>), 60%, 180-2.degree., iso-PrOH, PhCH<sub>2</sub>CO<sub>2</sub>Na; 8,1-Ph(hexyl), 30%, 240-2.degree., alc., BzONa, BzOEt.
- IT 98032-75-8, Xanthine, 8-(2-furyl)-1-hexyl-3-methyl-  
(prepn. of)
- RN 98032-75-8 HCPLUS
- CN Xanthine, 8-(2-furyl)-1-hexyl-3-methyl- (7CI) (CA INDEX NAME)



L5 ANSWER 162 OF 163 HCPLUS COPYRIGHT 2002 ACS  
 1962:73474 Document No. 56:73474 Original Reference No. 56:14264g-i,14265a-i,14266a-h Syntheses in the purine series. XIV. Properties and reactions of xanthine-8-aldehydes. Bredereck, Hellmut; Foehlisch, Baldur (Tech. Hochschule, Stuttgart, Germany). Chem. Ber., 95, 414-25 (Unavailable) 1962.

AB Xanthine-8-aldehydes showed typical aldehyde reactions. The CHO group underwent condensation reactions; in the presence of cyanide ions acyloin condensation to purine-acyloins (purinoins) took place. The R<sub>f</sub> values given throughout the abstr. were referred to picric acids; the same solvents were used as in the preceding abstr. 8-Hydroxymethyltheophylline (10.4 g.) in 25 cc. H<sub>2</sub>O and 35 cc. 2N NaOH treated with stirring with 10.5 g. KMnO<sub>4</sub> in 180 cc. H<sub>2</sub>O in about 5 portions below 40.degree., stirred 2-3 hrs. at room temp., and filtered, the residue washed with 100 cc. hot H<sub>2</sub>O, the combined filtrates shaken with C, heated, acidified with concd. HCl to pH 1, and refrigerated yielded 9.7 g. theophylline-8-carboxylic acid (I), needles, m. 273.degree. (H<sub>2</sub>O); the needles decarboxylated from about 210.degree. on with the formation of theophylline (II), m. 273.degree.. Theophylline-8-aldehyde (2 g.) in 20 cc. H<sub>2</sub>O and 6 cc. 2N NaOH treated with 1.03 g. KMnO<sub>4</sub> in 20 cc. H<sub>2</sub>O gave 1.21 g. II, m. 273.degree.. II (2 g.) in 200 cc. MeOH and 35 cc. 20-5% HCl-MeOH refluxed 8 hrs. and kept overnight yielded 1.41 g. Me ester (III) of II, needles, m. 253.degree. (with gas evolution); 0.12 g. 2nd crop. III (10.2 g.) and 40 cc. about 95% N<sub>2</sub>H<sub>4</sub>.H<sub>2</sub>O heated 6 hrs. on the water bath and evapd. in vacuo, the residue boiled with 200 cc. H<sub>2</sub>O and C, acidified hot with AcOH to pH 6-7, and refrigerated gave 9.3 g. (crude) hydrazide monohydrate of II, rhombs which decompd. slowly on heating. II (4 g.) and 40 cc. SOC<sub>12</sub> refluxed 4

hrs. with 5 drops C<sub>5</sub>H<sub>5</sub>N gave 3.9 g. crude acid chloride (IV) of II, brownish powder. Crude IV (0.8 g.) and 15 cc. concd. NH<sub>4</sub>OH kept 0.5 hr., boiled with 25 cc. H<sub>2</sub>O and C, acidified hot with AcOH to pH 4-5, and refrigerated overnight gave 0.47 g. amide (V) of II, yellowish crystals which did not melt up to 360.degree.. p-Dimethylaminophenylnitro (VI) (1 g.) of theophylline-8-aldehyde (VII) in 65 cc. 6N HCl and 0.4 g. NH<sub>2</sub>CONHNH<sub>2</sub>.HCl in 50 cc. 6N HCl kept 24 hrs. at room temp. gave 0.52 g. semicarbazone (VIII) of VII, powder, m. above 275.degree. (repptd. from dil. NH<sub>4</sub>OH with dil. HCl). VII (6.25 g.) in 100 cc. HCONMe<sub>2</sub> treated at 130.degree. with stirring with 2.8 g. H<sub>2</sub>NCSNH<sub>2</sub> (IX) in hot H<sub>2</sub>O and then with 3 drops concd. HCl, stirred 1 hr. at 130.degree., and filtered yielded 7.6 g. (crude) thiosemicarbazone monohydrate (X) of VII, yellowish microcryst. powder, m. 305.degree. (decompn.) (repptd. from dil. NH<sub>4</sub>OH with dil. HCl). VI (3.0 g.) in 195 cc. 6N HCl treated with 1 g. IX in 150 cc. dil. HCl, kept 3-4 hrs. at room temp., and filtered gave 2.1 g. X, m. 305.degree.; it lost the H<sub>2</sub>O on heating 3 days at 160.degree. over P<sub>2</sub>O<sub>5</sub>. VII (4.0 g.) in 20 cc. 40% aq. NaHSO<sub>3</sub> and 20 cc. H<sub>2</sub>O treated with 2 cc. PhNH<sub>2</sub> and 10 cc. AcOH, heated 15 min. on the steam bath, cooled, and filtered yielded 5.1 g. (crude) phenylhydrazone (XI) of VII, microscopic leaflets, decompd. above 285.degree. (BuOH). VI (0.23 g.) in 15 cc. 6N HCl treated with 150 mg. 2,4-(O<sub>2</sub>N)C<sub>6</sub>H<sub>3</sub>NH<sub>2</sub> in 10 cc. hot 6N HCl and filtered gave 0.21 g. 2,4-dinitrophenylhydrazone of VII, yellow powder from EtOH; it did not melt. VII (0.5 g.) in 35 cc. refluxing dioxane treated with 0.33 g. isonicotinic acid hydrazide in hot dioxane, treated with a trace of concd. HCl, refluxed 2 hrs., kept overnight, and filtered, and the residue dissolved in 2N NaOH, boiled with C, and repptd. dropwise with 50 cc. hot 10% aq. AcOH yielded 0.59 g. isonicotinic acid hydrazone (XII) of VII, yellow needles which did not melt. VII (1.0 g.) in refluxing dioxane treated with 0.34 g. NH<sub>2</sub>OH.HCl and 0.26 g. Na<sub>2</sub>CO<sub>3</sub> in 10 cc. H<sub>2</sub>O, heated 45 min. on the water bath, kept overnight, and filtered gave 0.55 g. oxime (XIII) of VII, decompd. on heating; 0.42 g. 2nd crop. VII (6 g.) in 80 cc. warm HCONMe<sub>2</sub> treated with 5 g. 1,3-dimethyl-4,5-diaminouracil in 20 cc. warm HCONMe<sub>2</sub>, heated 20 min. at 120-30.degree., cooled, dild. with 50 cc. H<sub>2</sub>O, kept overnight, and filtered yielded 10.1 g. 1,3-dimethyl-4-amino-5-(8-theophyllinylmethylenamino)uracil-2H<sub>2</sub>O (XIV.2H<sub>2</sub>O), brilliant yellow needles which did not melt; XIV.2H<sub>2</sub>O kept 2 days at 150.degree. over P<sub>2</sub>O<sub>5</sub> gave XIV. Theobromine-8-aldehyde (XV) (100 mg.) in 10 cc. hot AcOH treated with 100 mg. IX in 10 cc. H<sub>2</sub>O, kept overnight, and filtered yielded 130 mg. thiosemicarbazone monohydrate (XVI) of XV, cream-colored powder which did not melt. 3-Methylxanthine-8-aldehyde (XVII) and IX gave in the usual manner the thiosemicarbazone monohydrate of XVII, microscopic rodlets which decompd. gradually on heating. XIII (0.68 g.) in 75 cc. AcOH and 7 cc. Ac<sub>2</sub>O refluxed 15 min., kept 12 hrs., and filtered gave 0.58 g. O-acetate (XVIII) of XIII, microscopic rodlets, m. 287.degree. after sintering at about 200.degree. and elimination of AcOH (AcOH). XVIII (0.81 g.) heated with occasional stirring to 205-10.degree., cooled after 20 min., dild. with Et<sub>2</sub>O, and filtered yielded 0.61 g. (crude) 8-cyanotheophylline, m. 300.degree. (decompn.) (EtOH). XV (0.5 g.) in 35 cc. hot dioxane treated in the usual manner with 0.17 g. NH<sub>2</sub>OH.HCl and 0.13 g. Na<sub>2</sub>CO<sub>3</sub> gave 0.46 g. aldoxime (XIX) of XV; it did not melt. XIX (0.9 g.), 70 cc. AcOH, and 7 cc. Ac<sub>2</sub>O refluxed 15 min., concd. to remove 20 cc. distillate, kept overnight, and filtered yielded 0.91 g. O-acetate (XX) of XIX, needles, m. 279.degree. with sintering from about 210.degree. and elimination of AcOH. XX (0.9 g.) decompd. thermally gave 0.62 g. 8-cyanotheobromine, microcryst. powder, m. 287-8.degree. with sublimation (sublimed at 270-80.degree.). VII (1 g.) and 0.53 g. CH<sub>2</sub>(CO<sub>2</sub>H)<sub>2</sub> in 30 cc. dry C<sub>5</sub>H<sub>5</sub>N heated on the water bath, treated with 4 drops piperidine, heated 4-5 hrs. on the water bath, and evapd. in vacuo, the residue dissolved in 20 cc. H<sub>2</sub>O and 2 cc. N NaOH, treated with C, acidified hot with 5 cc. concd. HCl in 20 cc. hot H<sub>2</sub>O,

cooled, and filtered gave 0.2 g. 8-theophyllinylacrylic acid (XXI), needles, decompd. above 320.degree. (AcOH). VII (1 g.) and 0.77 g. CH<sub>2</sub>(CO<sub>2</sub>Et)<sub>2</sub> in 25 cc. abs. C<sub>5</sub>H<sub>5</sub>N heated on the steam bath, treated with 2 drops piperidine, heated 3 hrs., and evapd., and the residue triturated with 10 cc. EtOH, treated with a few drops AcOH, and refrigerated gave 1 g. 8-(2,2-dicarbethoxyvinyl)theophylline (XXII), needles, m. 216.degree. (decompn.) (EtOH). VII (1 g.), 1.1 g. BzCH<sub>2</sub>, 25 cc. dry C<sub>5</sub>H<sub>5</sub>N, and 2 drops piperidine heated 3 hrs. at 100.degree. gave similarly 0.74 g. (crude) 8-(2,2-dibenzoylvinyl)theophylline (XXIII), yellow needles which did not melt. VII (1.0 g.) and 0.48 g. Ac<sub>2</sub>CH<sub>2</sub> in 25 cc. C<sub>5</sub>H<sub>5</sub>N with 2 drops piperidine yielded 0.29 g. (crude) 8-(2,2-diacetylvinyl)theophylline (XXIV), yellowish needles which did not melt (EtOH). VII (1.0 g.), 0.93 g. BzCH<sub>2</sub>CO<sub>2</sub>Et, 25 cc. C<sub>5</sub>H<sub>5</sub>N, and 2 drops piperidine gave 0.91 g. (crude) 8-(2-benzoyl-2-carbethoxyvinyl)theophylline (XXV), needles, m. 238.degree. (decompn.) (EtOH). VII (1 g.), 0.78 g. AcBzCH<sub>2</sub>, 25 cc. dry C<sub>5</sub>H<sub>5</sub>N; and 2 drops piperidine yielded 0.66 g. 8-(2-acetyl-2-benzoylvinyl)theophylline (XXVa), yellow needles, m. 258.degree. (sintering and decompn.) (EtOH). VII (1 g.) and 0.75 g. 1,3-dimethylbarbituric acid (XXVI) in 25 cc. dry C<sub>5</sub>H<sub>5</sub>N refluxed 5 min., kept several hrs., and filtered gave 1.07 g. 1,3-dimethyl-5-(8-theophyllinylmethylene)barbituric acid, orange prisms from AcOH; it did not melt. VII (1 g.) and 0.837 g. 3-methyl-1-phenyl-5-pyrazolone (XXVII) in 25 cc. C<sub>5</sub>H<sub>5</sub>N refluxed 0.5 hr. and refrigerated overnight gave 1.16 g. 3-methyl-1-phenyl-4-(8-theophyllinylmethylene)-5-pyrazolone (XXVIII), deep red leaflets; it did not melt. VII (1 g.) and 1.13 g. 1,3-diphenyl-5-pyrazolone in 20 cc. dry C<sub>5</sub>H<sub>5</sub>N refluxed 0.5 hr. yielded 1.85 g. 3-Ph analog of XXVIII, brown-red, microscopic rodlets; it did not melt. VII (1.0 g.) and 0.64 g. rhodanine gave similarly 1.16 g. 8-theophyllinylmethylene-rhodanine, yellow crystals; it did not melt. XV (1 g.) and 0.75 g. XXVI in 25 cc. dry C<sub>5</sub>H<sub>5</sub>N refluxed 45 min. yielded 1.61 g. 1,3-dimethyl-5-(8-theobrominylmethylene)barbituric acid, yellow crystals from AcOH; it did not melt. XV(1 g.) and 0.83 g. XXVII gave in the usual manner 1.72 g. 8-theobrominyl analog of XXVIII, microscopic, rust-red crystals from boiling HCONMe<sub>2</sub>; it did not melt. VII (0.4 g.) in 30 cc. boiling dry dioxane treated with 2.1 g. Ph<sub>3</sub>P:CHCO<sub>2</sub>Et, refluxed 7 hrs., concd. to 1/3 vol., kept overnight, and filtered gave 0.16 g. Et ester of XXI, m. 257.degree. with previous sintering (EtOH). Caffeine-8-aldehyde (0.9 g.) in 30 cc. EtOH treated with stirring with 90 mg. KCN in 1 cc. H<sub>2</sub>O, dild. with 30 cc. EtOH, refluxed 15 min. with stirring, and filtered hot yielded 0.68 g. 1,2-dihydroxy-1,2-di(8-caffeinyl)ethylene (caffeinoin), lemon-yellow microscopic needles, decompd. from 285.degree.. XV (1 g.) in 50 cc. HCONMe<sub>2</sub> treated with stirring on the water bath with 100 mg. KCN in 1 cc. H<sub>2</sub>O, stirred 15 min. at 100.degree., and centrifuged gave 0.71 g. 1,2-dihydroxy-1,2-di(8-theobrominyl)ethylene (theobrominoi), yolk-yellow microcrystals which decompd. gradually on heating. VII (1 g.) in 15 cc. H<sub>2</sub>O and 2.5 cc. 2N NaOH treated with 100 mg. KCN in 1 cc. H<sub>2</sub>O, evapd. on the steam bath, dild. with 50 cc. H<sub>2</sub>O, treated with solid NH<sub>4</sub>Cl, boiled until pH 6 was reached, and filtered gave 0.73 g. 1,2-dihydroxy-1,2-di(8-theophyllinyl)ethylene, orange yellow, microscopic rodlets; it did not melt. The R<sub>f</sub> values with solvent A and the fluorescence color at 365 and 254 m.mu., and the same data obtained with solvent B given: I, 0.21, weak blue (at 254 m.mu.), 0.26, weak blue (at 254 m.mu.); III 0.62, brilliant blue (at 254 m.mu.), 0.53, brilliant blue (at 254 m.mu.); V, -, -, 0.26, weak blue; X, 0.26, dark blue, -, -; VIII, 0.26, brilliant blue, 0.19, brilliant blue; XI, 0.81, green-yellow, 0.67, green-yellow; XIII, -, -, 0.57, weak blue; XII, 0.32, gray-blue, -, -; XIV, 0.08, green-blue, 0.06, green-blue; XVI, 0.15, dark blue, 0.14, dark blue; XIX, 0.37, weak blue, 0.42, weak blue; XVIII, 0.68, weak blue (at 254 m.mu.), 0.74, weak blue (at 254 m.mu.); XX, 0.59, weak blue (at 254 m.mu.), 0.59, weak blue (at 254 m.mu.); XXI, 0.65, brilliant blue, 0.21, brilliant blue; XXII, 0.86,

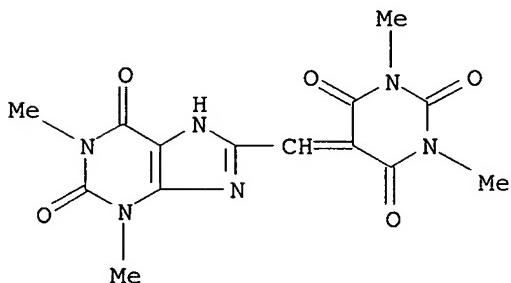
brilliant blue, 0.83, brilliant blue; XXIII, 0.98, yellow-green (at 365 m.mu.) (green at 254 m.mu.), 0.86, yellow-green (at 365 m.mu.) (green at 254 m.mu.); XXIV, 0.85, green-blue, 0.70, green-blue; XXV, 0.93, blue (at 365 m.mu.) (green-blue at 254 m.mu.), 0.86, blue (at 365 m.mu.) (green-blue at 254 m.mu.); XXVa, 0.94, yellow-green (at 365 m.mu.) (green at 254 m.mu.), 0.79, yellow-green (at 365 m.mu.) (green at 254 m.mu.). The ultraviolet absorption max. of the same compds. are tabulated.

IT 92495-37-9, Barbituric acid, 1,3-dimethyl-5-[(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)methylene]- 95071-66-2, Theophylline, 8-[(4-oxo-2-thioxo-5-thiazolidinylidene)methyl]- 98175-24-7, Theophylline, 8,8'-(dihydroxyvinylene)di-

98656-27-0, Theophylline, 8-[(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-ylidene)methyl]- 100410-66-0, Theophylline, 8-[(5-oxo-1,3-diphenyl-2-pyrazolin-4-ylidene)methyl]- (prepn. of)

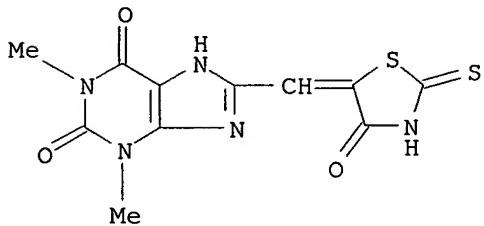
RN 92495-37-9 HCPLUS

CN Barbituric acid, 1,3-dimethyl-5-[(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurin-8-yl)methylene]- (7CI) (CA INDEX NAME)



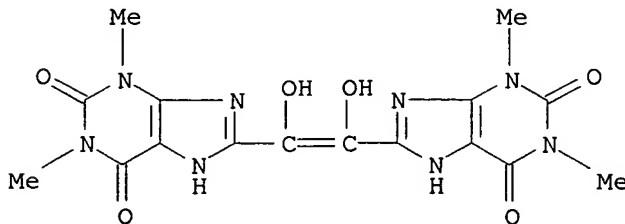
RN 95071-66-2 HCPLUS

CN Theophylline, 8-[(4-oxo-2-thioxo-5-thiazolidinylidene)methyl]- (7CI) (CA INDEX NAME)

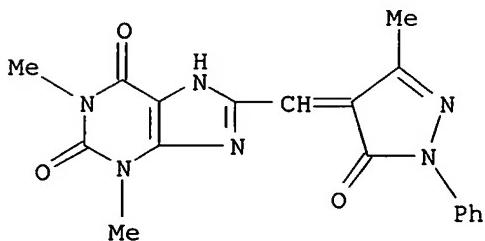


RN 98175-24-7 HCPLUS

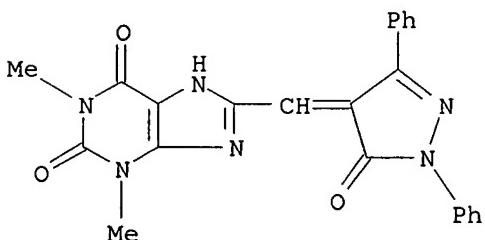
CN Theophylline, 8,8'-(dihydroxyvinylene)di- (7CI) (CA INDEX NAME)



RN 98656-27-0 HCPLUS  
CN Theophylline, 8-[(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-ylidene)methyl]-  
(7CI) (CA INDEX NAME)



RN 100410-66-0 HCPLUS  
CN Theophylline, 8-[(5-oxo-1,3-diphenyl-2-pyrazolin-4-ylidene)methyl]- (7CI)  
(CA INDEX NAME)



L5 ANSWER 163 OF 163 HCPLUS COPYRIGHT 2002 ACS  
1962:73473 Document No. 56:73473 Original Reference No. 56:14262h-i, 14263a-i, 14264a-g Syntheses in the purine series. XIII. The preparation of several xanthine-8-aldehydes. Bredereck, Hellmut; Siegel, Edgar; Foehlisch, Baldur (Tech. Hochschule, Stuttgart, Germany). Chem. Ber., 95, 403-13 (Unavailable) 1962.

AB cf. CA 56, 12891i. 8-Hydroxymethylxanthines (I) with  $\text{SOCl}_2$  yield the 8-chloromethylxanthines, the pyridinium salts of which can be converted with  $p\text{-Me}_2\text{NC}_6\text{H}_4\text{NO}$  (II) into nitrones. The HCl salts of theophylline-8-aldehyde nitrone (III) and the theobromine-8-aldehyde  $p$ -dimethylaminophenyl nitrone (IV) yield the corresponding 8-aldehydes. A simple synthesis of the xanthine-8-aldehydes consists in the oxidn. of I with  $\text{Na}_2\text{Cr}_2\text{O}_7$  in AcOH. All Rf values reported in this abstr. are referred to picric acid 0.55 (2:1 BuOH-5N AcOH, solvent A) and 0.83 (PrOH-1% aq.  $\text{NH}_4\text{OH}$ , solvent B). 3-Methyl-4,5-diaminouracil (8.3 g.) and 8.5 g. cryst.  $\text{HOCH}_2\text{CO}_2\text{H}$  ground together, heated 1 hr. on the water bath, cooled, dild with 55 cc.  $\text{H}_2\text{O}$ , neutralized with solid NaOH, treated with 55 cc. 2N NaOH, refluxed 2.5 hrs., filtered, acidified with  $\text{H}_2\text{SO}_4$  to pH 4, and refrigerated gave 5.8 g. 3-methyl-8-hydroxymethylxanthine (V), decompd. from about 300.degree. ( $\text{H}_2\text{O}$ ). V (1.3 g.) in 3.5 cc. 2N NaOH and 8 cc.  $\text{H}_2\text{O}$  heated to 40.degree., treated with 0.88 cc.  $\text{Me}_2\text{SO}_4$  in 5 cc. MeOH, adjusted dropwise with 2N NaOH at 40.degree. to a const. pH of 7-7.5, refrigerated, and filtered yielded 0.85 g. 8-hydroxymethyltheobromine (VI), m. 297.degree. ( $\text{H}_2\text{O}$ ), Rf 0.39 (A), 0.59 (B). Caffeine (12 g.), 12 g. paraformaldehyde, 18 cc. AcOH, and 6 cc. concd. HCl heated 17 hrs. at 160-70.degree. in a sealed tube, adjusted with strong aq. NaOH to pH 6, and extd. 10 hrs. with 250 cc.  $\text{CHCl}_3$ , and the ext. concd. to 100 cc. and refrigerated gave 5 g. 8-hydroxymethylcaffeine (VII), m. 225.degree.

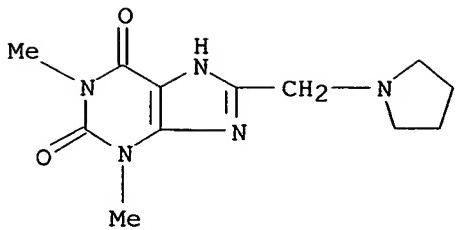
(EtOH). VI (0.7 g.), 3.5 cc. SOC<sub>12</sub>, and 2 drops C<sub>5</sub>H<sub>5</sub>N refluxed 6 hrs. and evapd. yielded 0.7 g. 8-chloromethyltheobromine (VIII), m. 263.degree. (dioxane). 8-Hydroxymethyltheophylline (IX) (15.1 g.) treated with cooling with 45 cc. SOC<sub>12</sub> and 3-5 drops C<sub>5</sub>H<sub>5</sub>N, kept 0.5 hr., refluxed 4 hrs., and evapd. gave 14.9 g. 8-chloromethyltheophylline (X), m. 241.degree. (dry dioxane). V (1 g.), 10 cc. SOC<sub>12</sub>, and 2 drops C<sub>5</sub>H<sub>5</sub>N gave similarly 0.92 g. 8-ClCH<sub>2</sub> analog (XI) of V, prisms from dioxane; it did not melt. X (3.43 g.) in 150 cc. abs. EtOH refluxed 15 hrs. with 2.5 g. dry pyrrolidine, concd. to about 10 cc., refrigerated, and filtered, and the residue dissolved in 25 cc. boiling MeOH, concd. to 3-5 cc., and cooled yielded 1.9 g. 8-pyrrolidinylmethyltheophylline (XII), needles, m. 203.degree.; 0.3 g. 2nd crop. XII (0.26 g.) in 1 cc. concd. NH<sub>4</sub>OH treated with 0.2 g. AgNO<sub>3</sub> in 0.5 cc. H<sub>2</sub>O pptd. 0.35 g. Ag salt of XII. XI (0.21 g.) and 0.37 g. PhNHCH<sub>2</sub>Ph (XIII) heated 12 hrs. under a stream of dry N at 150.degree., cooled, powd., boiled 3 times with 3-cc. portions H<sub>2</sub>O, and filtered hot gave 0.15 g. 3-methyl-8-(N-benzylanilinomethyl)xanthine, platelets, m. 250.degree. (aq. HCONMe<sub>2</sub>). X (0.23 g.) and 0.37 g. XIII in 10 cc. abs. EtOH refluxed 15 hrs., cooled, and filtered yielded 0.31 g. 8-(N-benzylanilinomethyl)theophylline, prisms, m. 206.degree. (EtOH-dioxane). 8-Chloromethylcaffeine (0.24 g.) in 0.37 g. XIII and 10 cc. abs. EtOH gave similarly 0.21 g. 8-(N-benzylanilinomethyl)caffeine, m. 156.degree. (aq. dioxane). XII (0.53 g.) in 10 cc. abs. EtOH treated with 46 mg. Na in 2.5 cc. abs. EtOH, then treated dropwise with cooling with 0.36 g. p-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl in 2 cc. abs. EtOH, kept 1 hr. at room temp., refluxed 4 hrs., filtered hot, concd., neutralized with a few drops AcOH, and filtered gave 0.2 g. 8-ethoxymethyltheophylline, needles from 3:2 dioxane-H<sub>2</sub>O; it did not melt. IX (5.6 g.) added with stirring to 1.07 g. NaOH in 15 cc. H<sub>2</sub>O, treated with 135 cc. 96% EtOH, cooled, treated dropwise with 4.86 g. p-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl in 25 cc. 96% EtOH with cooling and stirring during 10 min., warmed slowly to 20.degree., refluxed about 13 hrs. with stirring, filtered hot, concd. to 30-50 cc., cooled, and filtered, and the residue stirred 3 min. with 10 cc. concd. NH<sub>4</sub>OH and filtered gave 4.8 g. 7-(p-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>) deriv. (XIV) of IX, needles, m. 217.degree. (EtOH). XIV (4.7 g.) and 13 cc. SOC<sub>12</sub> refluxed 6 hrs. and evapd. in vacuo, the residue treated with 5 cc. MeOH and evapd., the crude product extd. with 20 cc. boiling CHCl<sub>3</sub>, and the ext. evapd. gave 3.3 g. 7-(p-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>) deriv. (XV) of X, needles, m. 170.degree. (abs. EtOH). XV (2.9 g.) in 100 cc. abs. EtOH treated with 1.3 g. pure dry pyrrolidine, refluxed 15 hrs., concd. to 10 cc., and refrigerated gave 2.57 g. 7-(p-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>) deriv. (XVI) of XII, m. 149.degree.. XVI (2.4 g.) in 5 cc. H<sub>2</sub>O treated with 2 cc. 6N HCl, dild. with 15 cc. H<sub>2</sub>O, and boiled briefly with C yielded 2.4 g. XVI.HCl, needles, m. 227.degree.. X (1 g.) in 15 cc. dry C<sub>5</sub>H<sub>5</sub>N kept at room temp., refrigerated, and filtered yielded 1.2 g. N-(8-theophyllinylmethyl)pyridinium chloride (XVII); it did not show a definite m.p. VIII (0.7 g.) and 14 cc. dry C<sub>5</sub>H<sub>5</sub>N heated about 20 min. on the water bath, kept overnight at room temp., concd. in vacuo to 1 cc., dild. with 5 cc. Et<sub>2</sub>O, refrigerated, and filtered gave 0.89 g. 8-theobrominylmethyl analog (XVIII) of XVII, prisms, m. 288-90.degree.. XI (0.6 g.) and 9 cc. dry C<sub>5</sub>H<sub>5</sub>N gave similarly 0.7 g. N-(3-methyl-8-xanthinylmethyl) analog (XIX) of XVII, prisms; it did not melt. 8-Chloromethylcaffeine (1 g.) and 20 cc. dry C<sub>5</sub>H<sub>5</sub>N heated briefly on the water bath, kept 1 hr. at room temp., and filtered gave 0.41 g. 8-caffeinylmethyl analog (XX) of XVII, needles, m. 248.degree. (EtOH). XVIII (0.74 g.) in 2 cc. H<sub>2</sub>O and 11 cc. hot EtOH treated with 0.36 g. II and 2.42 cc. N NaOH and kept overnight gave 0.67 g. IV, rust-brown prisms (4:1 EtOH-H<sub>2</sub>O). XVII (0.62 g.) in 2 cc. H<sub>2</sub>O and 10 cc. EtOH treated with 0.3 g. II, kept 36 hrs. at 40.degree., and refrigerated yielded 0.37 g. III, golden crystal powder, m. 270.degree. with effervescence (on rapid heating). XIX (0.39 g.) in 1 cc. H<sub>2</sub>O and 2 cc. EtOH treated with 0.22 g. II and 1.32 cc. N NaOH and kept 5 days at room temp. yielded 0.24 g.

3-methylxanthine-8-aldehyde analog of IV, reddish brown prisms, m. 255-60.degree. (decompn.) (1:1 HCONMe<sub>2</sub>-H<sub>2</sub>O). XX (0.76 g.) in 1 cc. H<sub>2</sub>O and 10 cc. EtOH with 0.39 g. II and 1.2 cc. 2N NaOH yielded 0.1 g. caffeine-8-aldehyde analog of IV, yellow needles, m. 195.degree. (decompn.) (on slow heating) (EtOH). IV (0.34 g.) ground with cooling with 1 cc. concd. HCl and filtered, the residue washed with abs. EtOH, boiled briefly with 4 cc. H<sub>2</sub>O, cooled, and filtered yielded 0.14 g. theobromine-8-aldehyde (XXI), needles, m. 286.degree. (dioxane) (on rapid heating), Rf 0.64 (A), 0.40 (B), weak blue fluorescence. VI (1 g.) in 40 cc. AcOH treated dropwise during 1 hr. at 80-5.degree. with 0.55 g. Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>.2H<sub>2</sub>O in 25 cc. warm AcOH, stirred 0.5 hr. at 80-5.degree., concd., dild. with 10 cc. H<sub>2</sub>O, and filtered gave 0.69 g. XXI, m. 286-8.degree. (decompn.) (dioxane). III (0.8 g.) ground with 2 cc. concd. HCl, stirred with 15 cc. Me<sub>2</sub>CO, kept 15 min. at 0.degree., and filtered gave 0.11 g. theophylline-8-aldehyde (XXII); it did not melt, but decompd. IX (20 g.) in 400 cc. AcOH treated with stirring at 80-5.degree. with 10 g. powd. Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>.2H<sub>2</sub>O in portions during 15 min., stirred 0.5 hr. at 80-5.degree., kept overnight, and filtered yielded 11.9 g. XXII, Rf 0.55 (B), weak blue fluorescence. V (1.5 g.) in 100 cc. AcOH treated at 80-5.degree. with 0.73 g. powd. Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>.2H<sub>2</sub>O gave 1.1 g. (crude) 3-methylxanthine-8-aldehyde, yellow crystal powder, decompd. above 200.degree., Rf 0.31 (A), 0.37 (B), weak blue fluorescence. VII (2.24 g.) in 50 cc. AcOH treated at 80-5.degree. with 1.05 g. Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>.2H<sub>2</sub>O in 40 cc. AcOH gave 1.45 g. caffeine-8-aldehyde, yellowish needles, m. 165-9.degree. (EtOAc), Rf 0.79 (A), 0.86 (B). IX (4.1 g.) in 10 cc. 2N NaOH evapd. in vacuo, the residue triturated with Me<sub>2</sub>CO and filtered, the dried residue stirred 4 hrs. at 120-40.degree. with 4.2 g. BzCH<sub>2</sub>Br in 50 cc. dry HCONMe<sub>2</sub>, and evapd. in vacuo, and the residue triturated with H<sub>2</sub>O gave 6.0 g. (crude) 7-BzCH<sub>2</sub> deriv. (XXIII) of IX, m. 251.degree. (MeOCH<sub>2</sub>CH<sub>2</sub>OH). XXIII (0.98 g.) in 40 cc. AcOH with 3.2 g. Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>.2H<sub>2</sub>O yielded 0.65 g. (crude) 7-BzCH<sub>2</sub> deriv. of XXII, m. 239.degree. with sintering, which recrystd. from 40 parts BuOH gave needles contg. 1 mole crystal BuOH, m. 242.degree. with sintering from 218.degree.. 1,3-Dibenzyl-4,5-diaminouracil (XXIV) (1.16 g.) and 0.8 g. cryst. HOCH<sub>2</sub>CO<sub>2</sub>H heated 1 hr. on the water bath gave 1.28 g. 1,3-dibenzyl-4-amino-5-(hydroxyacetamino)uracil (XXV), needles, m. 243.degree. (dioxane). XXIV (1.0 g.) and 2 cc. HOCH<sub>2</sub>CO<sub>2</sub>Et heated at 145-55.degree., cooled, dild. with 15 cc. Et<sub>2</sub>O, and refrigerated gave 0.84 g. XXV, m. 216.degree.. XXV (16 g.) and 10 g. cryst. HOCH<sub>2</sub>CO<sub>2</sub>H heated 1 hr. on the water bath, cooled, ground with 200 cc. 50% aq. EtOH, basified with solid NaOH, refluxed 2.5 hrs. with 7 g. NaOH, filtered hot, acidified with AcOH, refrigerated, and filtered gave 13.3 g. (crude) 1,3-dibenzyl-8-hydroxymethylxanthine (XXVI), m 210.degree. (EtOAc). XXVI (4.0 g.) in about 150 cc. dry liquid NH<sub>3</sub>, treated with Na in small pieces until the blue color persisted for at least 15 min., decompd. with solid NH<sub>4</sub>Cl, and evapd., the residue boiled with stirring with 50 cc. H<sub>2</sub>O, filtered hot, acidified with concd. HCl to pH 3-4, and cooled gave 1.7 g. 8-hydroxymethylxanthine, yellowish microscopic crystals, Rf 0.15 (A), 0.17 (B); it gave a pos. murexide reaction and a gelatinous ppt. with AgNO<sub>3</sub>-NH<sub>4</sub>OH.

IT 96434-28-5, Theophylline, 8-(1-pyrrolidinylmethyl)-  
(7-silver deriv.)

RN 96434-28-5 HCAPLUS

CN Theophylline, 8-(1-pyrrolidinylmethyl)- (7CI) (CA INDEX NAME)



(prep. of

=> log y  
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	724.78	759.18

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-100.98	-100.98

STN INTERNATIONAL LOGOFF AT 14:24:32 ON 03 DEC 2002